

## WEST Search History

DATE: Friday, November 22, 2002

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB= USPT,PGPB,JPAB,EPAB,DWPI; PLUR YES; OP ADJ</i>			
L14	L2 and L12	2	L14
L13	L1 and L12	0	L13
L12	GGGACTTTCC	64	L12
L11	L2 and L9	184	L11
L10	L1 and L9	101	L10
L9	binding sites	37632	L9
L8	L6 and L2	0	L8
L7	L6 and L1	1	L7
L6	L3 and L5	64	L6
L5	dendritic cell	3007	L5
L4	ribozym\$3	8755	L4
L3	tolerogen\$3	395	L3
L2	nf kappa b	424	L2
L1	nuclear factor kappa b	211	L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 11:34:48 ON 21 NOV 2002)

FILE 'BIONIS, MEDLINE, 'AIDS', ENBASE' ENTERED AT 11:34:50 ON 21 NOV 2002

L1 25547 NUCLEAR FACTOR KAPPA B  
L2 41469 NF KAPPA B  
L3 4421 TOLEROGEM  
L4 15153 RIBOZYME  
L5 183175 OLIGONUCLEOTIDE  
L6 77082 ANTISENSE  
L7 622 L1 AND L2  
L8 1 L1 AND L2  
L9 1 L1 AND L2  
L10 1 L1 AND L2  
L11 1 L1 AND L2  
L12 1 L1 AND L2  
L13 1 L1 AND L2  
L14 1 L1 AND L2  
L15 1 L1 AND L2  
L16 390 GENEALOGY CELL  
L17 44906 GENEALOGY CELL  
L18 1 L1 AND L2 AND L17  
L19 11 DUP REM L16 (1 DUPLICATE REMOVED)  
L20 31 L2 AND L5 AND L17  
L21 15 DUP REM L20 (6 DUPLICATES REMOVED)

FILE 'BIOSIS, MEDLINE, CAPLUS, ENBASE' ENTERED AT 11:45:15 ON 21 NOV 2002

L21 7 L17 AND L3 AND L1  
L22 5 DUP REM L21 (3 DUPLICATES REMOVED)  
L23 10 L17 AND L3 AND L1  
L24 6 DUP REM L23 (4 DUPLICATES REMOVED)  
L25 2 L1 AND L3 AND L1  
L26 11 L1 AND L3 AND L1

FILE 'BIOSIS, MEDLINE, CAPLUS, ENBASE' ENTERED AT 11:47:15 ON 21 NOV 2002

FILE 'BIOSIS, MEDLINE, CAPLUS, ENBASE' ENTERED AT 11:47:15 ON 21 NOV 2002

L27

FILE 'BIOSIS, MEDLINE, CAPLUS, ENBASE' ENTERED AT 11:47:15 ON 21 NOV 2002

L27 1 L1 AND L3 AND L1  
L28 81473 PINKISH JETTY  
L29 519 L1 AND L3  
L30 814 L2 AND L3  
L31 6 L31 AND L17  
L32 6 DUP REM L31 (6 DUPLICATES REMOVED)  
L33 8 L32 AND L17  
L34 8 DUP REM L33 (8 DUPLICATES REMOVED)

L35

134 ANSWER 1 OF 6 CARLISL. COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2001-0118 CARLISL

DOCUMENT NUMBER: 134:000000

TITLE: Selective expression of type 1 IFN genes in human **dendritic cells** infected with *Mycobacterium tuberculosis*

AUTHOR(S): Remoli, Maria Elena; Giacomini, Elena; Lutfalla, Georges; Dondi, Elisabetta; Orefici, Graziella; Battistini, Angela; Uze, Gilles; Pellegrini, Sandra; Cocchi, Eliana M.

CORPORATE SOURCE: Laboratories of Immunology, Institute Superiore di Sanita, Rome, 00161, Italy

SOURCE: Journal of Immunology 166:11, 1996-11, 306-314

ISSN: 0022-1767; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Type 1 IFN promotes different aspects of the immune response, inducing a cell-mediated immunity. We have recently shown that the infection of **dendritic cells** (DC) with *Mycobacterium tuberculosis* (Mtb) induces IFN-.alpha.. In this work we have monitored a rapid induction of IFN-.beta. followed by the delayed prodn. of the IFN-.alpha.1 and/or -.alpha.13 subtypes. The Mtb infection rapidly activates the NF-.kappa.B complex and stimulates the phosphorylation of IFN regulatory factor (IRF)-3, events known to induce IFN-.beta. expression in viral infection. In turn, the autocrine prodn. of IFN-.beta. induces the IFN-stimulated genes that contain **binding sites** for activated STATs in their promoters. Among the IFN-stimulated genes induced in DC through STAT activation are IRF-1 and IRF-7. The expression of IRF-1 appears to be dependent on the sequential activation of NF-.kappa.B and STAT-1. Once expressed, IRF-1 may further stimulate the transcription of IFN-.beta.. Induction of IRF-7 is also regulated at the transcriptional level through the binding of phosphorylated STAT-1 and STAT-2, forming the IFN-stimulated gene factor-3 complex. In turn, the IRF-1 and IRF-7 complex appears to be required for the delayed induction of the IFN-.alpha.13 subtypes. Although speculative, our results strongly support the existence of a cascade of events in Mtb-infected DC. Upon infection, constitutively expressed NF-.kappa.B and IRF-3 are activated and likely contribute to the rapid IFN-.beta. expression. In turn, IFN-.beta.-induced IRF-1 and IRF-7 may cooperate toward induction of IFN-.alpha.1/13. Infection persists and these factors are activated.

REFERENCE COUNT: 1 THERE ARE NO CITED REFERENCES AVAILABLE FOR THIS ENTRY. ALL CITATIONS AVAILABLE IN THE RE FORMAT

134 ANSWER 2 OF 6 CARLISL. COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2001-01647 CARLISL

DOCUMENT NUMBER: 134:000016

TITLE: The use of tolerogenic **dendritic cells** for enhancing tolerogenicity in a host and methods for making the same

INVENTOR(S): Robbins, Paul D.; Lu, Ling; Glenn Burke, Nick  
PATENT ASSIGNEE(S): University of Pittsburgh of the Commonwealth System of Higher Education, USA

SOURCE: J Clin Invest 107:11, 2001-11, 1300-1308

ISSN: 0021-9745

DOCUMENT TYPE: Journal

LANGUAGE: English

FAMILY NO. INFO. 2001-01647

PATENT INFORMATION:

PATENT NO.	FILE DATE	APPLICATION NO.	DATE
W 2001-01647	2001-01-11	W 2001-01647	2001-01-11
W 2001-01647	2001-01-11	W 2001-01647	2001-01-11

W: AE, AG, AI, AM, AT, AU, AV, BA, BB, BC, BD, BE, BF, CA, CB, CC, CD, CE, CF, CG, CH, CI, CJ, CK, CL, CM, CN, CO, CP, CQ, CR, CS, CT, CU, CV, CW, CX, CY, CZ, DA, DB, DC, DD, DE, DF, DG, DH, DI, DJ, DK, DL, DM, DN, DO, DP, DQ, DR, DS, DT, DU, DV, DW, DX, DY, DZ, EA, EB, EC, ED, EE, EF, EG, EH, EI, EJ, EK, EL, EM, EN, EO, EP, EQ, ER, ES, ET, EU, EV, EW, EX, EY, EZ, FA, FB, FC, FD, FE, FF, FG, FH, FI, FJ, FK, FL, FM, FN, FO, FP, FQ, FR, FS, FT, FU, FV, FW, FX, FY, FZ, GA, GB, GC, GD, GE, GF, GG, GH, GI, GJ, GK, GL, GM, GN, GO, GP, GQ, GR, GS, GT, GU, GV, GW, GX, GY, GZ, HA, HB, HC, HD, HE, HF, HG, HH, HI, HJ, HK, HL, HM, HN, HO, HP, HQ, HR, HS, HT, HU, HV, HW, HX, HY, HZ, IA, IB, IC, ID, IE, IF, IG, IH, II, IJ, IK, IL, IM, IN, IO, IP, IQ, IR, IS, IT, IU, IV, IW, IX, IY, IZ, JA, JB, JC, JD, JE, JF, JG, JH, JI, JJ, JK, JL, JM, JN, JO, JP, JQ, JR, JS, JT, JU, JV, JW, JX, JY, JZ, KA, KB, KC, KD, KE, KF, KG, KH, KI, KJ, KK, KL, KM, KN, KO, KP, KQ, KR, KS, KT, KU, KV, KW, KX, KY, KZ, LA, LB, LC, LD, LE, LF, LG, LH, LI, LJ, LK, LL, LM, LN, LO, LP, LQ, LR, LS, LT, LU, LV, LW, LX, LY, LZ, MA, MB, MC, MD, ME, MF, MG, MH, MI, MJ, MK, ML, MM, MN, MO, MP, MQ, MR, MS, MT, MU, MV, MW, MX, MY, MZ, NA, NB, NC, ND, NE, NF, NG, NH, NI, NJ, NK, NL, NM, NN, NO, NP, NQ, NR, NS, NT, NU, NV, NW, NX, NY, NZ, OA, OB, OC, OD, OE, OF, OG, OH, OI, OJ, OK, OL, OM, ON, OO, OP, OQ, OR, OS, OT, OU, OV, OW, OX, OY, OZ, PA, PB, PC, PD, PE, PF, PG, PH, PI, PJ, PK, PL, PM, PN, PO, PP, PQ, PR, PS, PT, PU, PV, PW, PX, PY, PZ, QA, QB, QC, QD, QE, QF, QG, QH, QI, QJ, QK, QL, QM, QN, QO, QP, QQ, QR, QS, QT, QU, QV, QW, QX, QY, QZ, RA, RB, RC, RD, RE, RF, RG, RH, RI, RJ, RK, RL, RM, RN, RO, RP, RQ, RR, RS, RT, RU, RV, RW, RX, RY, RZ, SA, SB, SC, SD, SE, SF, SG, SH, SI, SJ, SK, SL, SM, SN, SO, SP, SQ, SR, SS, ST, SU, SV, SW, SX, SY, SZ, TA, TB, TC, TD, TE, TF, TG, TH, TI, TJ, TK, TL, TM, TN, TO, TP, TQ, TR, TS, TU, TV, TW, TX, TY, TZ, UA, UB, UC, UD, UE, UF, UG, UH, UI, UJ, UK, UL, UM, UN, UO, UP, UQ, UR, US, UT, UU, UV, UW, UX, UY, UZ, VA, VB, VC, VD, VE, VF, VG, VH, VI, VJ, VK, VL, VM, VN, VO, VP, VQ, VR, VS, VT, VU, VV, VW, VX, VY, VZ, WA, WB, WC, WD, WE, WF, WG, WH, WI, WJ, WK, WL, WM, WN, WO, WP, WQ, WR, WS, WT, WU, WV, WW, WX, WY, WZ, XA, XB, XC, XD, XE, XF, XG, XH, XI, XJ, XK, XL, XM, XN, XO, XP, XQ, XR, XS, XT, XU, XV, XW, XX, XY, XZ, YA, YB, YC, YD, YE, YF, YG, YH, YI, YJ, YK, YL, YM, YN, YO, YP, YQ, YR, YS, YT, YU, YV, YW, YX, YY, YZ, ZA, ZB, ZC, ZD, ZE, ZF, ZG, ZH, ZI, ZJ, ZK, ZL, ZM, ZN, ZO, ZP, ZQ, ZR, ZS, ZT, ZU, ZV, ZW, ZX, ZY, ZZ.

US 2001-844915 20010427

PRIORITY APPL. INFO.: US 2000-200479P P 20000428

AB The present invention relates to a tolerogenic mammalian **dendritic cells** (DCs) and methods for the prodn. of the tolerogenic DCs. In addn., the present invention provides a method for enhancing tolerogenicity in a host comprising administering the tolerogenic mammalian DCs of the present invention to the host. The tolerogenic DCs of the present invention comprise an oligodeoxyribonucleotide (ODN) which has one or more NF- $\kappa$ B **binding sites**. The tolerogenic DCs of the present invention may further comprise a viral vector, and preferably an adenoviral vector, which does not affect the tolerogenicity of the tolerogenic DCs when present therein. Enhanced tolerogenicity in a host is useful for prolonging foreign graft survival and for treating inflammatory related diseases, such as autoimmune diseases.

L34 ANSWER 3 OF 4 (ARTICLE 17(2)(b) EPC)

ACCESSION NUMBER: 2001-04-11

DOCUMENT NUMBER: 2001-04-11

TITLE: **Enhancement of cardiac allograft survival using dendritic cells treated with NF- $\kappa$ B decoy oligodeoxyribonucleotides**

AUTHOR(s): Giannoukakis, Nick; Bonham, C. Andrew; Qian, Shiguang; Zhou, Zhongyou; Peng, Liansha; Harnaha, Jo; Li, Wei; Thomson, Angus W.; Fung, John J.; Robbins, Paul D.; Lu, Lina

CORPORATE SOURCE: Department of Molecular Genetics and Biochemistry, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: Molecular Therapy (2000), 1(5, Pt. 1), 436-447

CODEN: MTHCHK; ISSN: 1525-0016

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Dendritic cells** (DC) classically prime the immune responses for naive lymphocytes. Mature antigen-specific lymphocytes are induced by the expression of stimulatory molecules (CD40, CD80, CD86) on the surface of DCs. In addition, their capacity to induce tolerance is related to the expression of these molecules. DCs with NF- $\kappa$ B-dependent transcription of their genes. DCs treated with NF- $\kappa$ B-dependent transcriptional inhibitors (NF- $\kappa$ B-dependent transcriptional inhibitors) as well as NF- $\kappa$ B translocation to the nucleus. In this report, we demonstrate that double-stranded oligodeoxyribonucleotides (ODNs) **binding sites** for NF- $\kappa$ B NF- $\kappa$ B ODNs are efficiently incorporated by bone marrow-derived DCs and specifically inhibit NF- $\kappa$ B-dependent transcription of a reporter gene. Moreover, exposure of DC to the oligodeoxyribonucleotide (ODN)-induced nitric oxide prodn., a marker of DC maturation. Treatment of bone marrow-derived DC progenitors with NF- $\kappa$ B ODNs selectively suppresses the cell-surface expression of stimulatory molecules and interferes with MHC class II expression. Furthermore, NF- $\kappa$ B ODNs induce allogeneic DC-specific suppression of T cell proliferation in mixed lymphocyte cultures, and this was associated with induction of CD40L and CD80L. Finally, induction of NF- $\kappa$ B ODNs in bone marrow-derived DCs and subsequent administration of these cells to mice with diabetes mellitus

significant prolongation of allograft survival in the absence of immunosuppression. Specific interference with NF- $\kappa$ B and other transcriptional pathways involved in immune stimulation in LC using GDN decoy approaches could be one means to promote tolerance induction in organ transplantation. (c) 2000 Academic Press.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REF FORMAT

134 AMMER, G. P. / JOURNAL OF IMMUNOLOGY, 160(3), 1224-1232

ACCESSION NUMBER: 19980101000000000000

DOCUMENT NUMBER: 19980101000000000000

TITLE: Vascular endothelial growth factor affects

dendritic cell maturation through

the inhibition of nuclear factor-

$\kappa$ B activation in hemopoietic

progenitor cells

AUTHOR(S): Yama, Tsunenori; Ran, Sophia; Ishida, Tadao; Nadaf, Sarena; Kerr, Lawrence; Carbone, David P.; Gribilovich, Dmitry I.

CORPORATE SOURCE: The Vanderbilt Cancer Center and Departments of Medicine and Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN, 37232, USA

SOURCE: Journal of Immunology (1998), 160(3), 1224-1232

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vascular endothelial growth factor (VEGF), produced by almost all tumor cells, affects the ability of hemopoietic progenitor cells (HPC) to differentiate into functional dendritic cells (DC). During the early stages of tumor metastasis, in this study we demonstrate specific binding of VEGF to HPC. This binding was efficiently competed by placenta growth factor (PlGF), a ligand reportedly specific for the Flt-1 receptor. The number of binding sites for VEGF decreased during differentiation in vitro, associated with decreased levels of mRNA for Flt-1. VEGF significantly inhibited nuclear factor-

$\kappa$ B (NF- $\kappa$ B)-dependent activation of reporter

gene transcription during the first 24 h in culture. The presence of VEGF significantly decreased the specific DNA binding of NF- $\kappa$ B as early as 30 min after induction with TNF- $\alpha$ . This was followed on days 7 to 10 by decreases in the mRNA for RelB and c-Rel, two subunits of NF- $\kappa$ B. Blockade of NF- $\kappa$ B activity in HPC at early stages of differentiation with an adenovirus expressing a dominant  $\kappa$ B inhibitor of NF- $\kappa$ B reproduced the pattern of attenuated, with VEGF. Thus, NF- $\kappa$ B plays an important role in maturation of HPC to DC, and VEGF activation of the Flt-1 receptor is able to block the activation of NF- $\kappa$ B in this system. Blockade of NF- $\kappa$ B activation in HPC by tumor-derived factors may therefore be a mechanism by which tumor cells can directly suppress the ability of the immune system to respond against the tumor cells.

134 AMMER, G. P. / JOURNAL OF IMMUNOLOGY, 160(3), 1224-1232

ACCESSION NUMBER: 19980101000000000000

DOCUMENT NUMBER: 19980101000000000000

TITLE: NF- $\kappa$ B activation by IL-1 promotes nuclear translocation of NF- $\kappa$ B and primes it for IL-1 production

AUTHOR(S): Brennan, Thomas; Bellaschi, Maria L.; Bianchi, Roberto; Luciani, Fabiana; Ayoubi, Farid; Fioravanti, Maria L.; Iscra, Luigi

CORPORATE SOURCE: Department of Experimental Medicine, University of Perugia, Perugia, Italy, Italy

SOURCE: Immunity (1998), 8(3), 415-424

the 1990s, the number of people in the world who are under 15 years of age is expected to increase from 1.1 billion to 1.5 billion. The number of people aged 65 and over is expected to increase from 200 million to 400 million. The number of people aged 15 and over is expected to increase from 3.5 billion to 4.5 billion. The number of people aged 15 and over is expected to increase from 3.5 billion to 4.5 billion. The number of people aged 15 and over is expected to increase from 3.5 billion to 4.5 billion.

REFERENCE COUNT: 48 THERE ARE 48 OTHER REFERENCES AVAILABLE FOR THIS  
 SUBJECT. ALL CITATIONS AVAILABLE IN THE REFERENCE

AB Interleukin-12 is produced in response to infection with bacteria or parasites or to bacterial components such as lipopolysaccharide (LPS) in monocytes/macrophages and **dendritic cells**, and is generated by the interaction between activated T cells and antigen-presenting cells via CD-28-CD28 ligand, CD40-CD40L. Transcriptional analysis of p40 was carried out using various bacteria, components such as LPS or flag-tagged bacterial components, stimulation of p40 by CD-28 ligation was characterized using murine B lymphoma cell lines, J458, J459, and a human monocytic cell line, THP-1. These cells, stimulated by an agonist or a component of bacteria, induced CD-28 or by transfection with a CD40L expression vector, induced p40 mRNA expression. Sequence analysis of p40 promoter revealed a forkhead, potential nuclear factor- $\kappa$ B (NF- $\kappa$ B) binding sites, and pre-identified murine and human NF- $\kappa$ B promoter activity shift assay revealed that the potential NF- $\kappa$ B binding sequence which is located around 120 bp upstream of the transcription initiation site in murine and human p40 genes formed an NF- $\kappa$ B complex with nuclear ext. from Daudi cells stimulated by CD-28 ligation. Moreover, transfection of Daudi cells with the polymd. NF- $\kappa$ B binding sequence ligated to a thymidine kinase/chloramphenicol acetyltransferase (CAT) reporter plasmid greatly induced CAT activity, but transfection with the polymd. mutated NF- $\kappa$ B binding sequence did not. These results suggest that the NF- $\kappa$ B binding site is involved in the regulation of the transcriptional induction of p40 in murine and human cells, and is a candidate for the p40 promoter. CD-28-CD40L interaction is of NF- $\kappa$ B.

136 ANSWER 1 OF 7 MARION COPYRIGHT 2002 A.A.I.M.

ACCESSION NUMBER: 2002:712316 CAPLUS

TITLE: Marked prolongation of cardiac allograft survival by **dendritic cells** genetically engineered with NF- $\kappa$ .

AUTHOR(S): Berman, J. Andrew; Bhat, Indira; Liang, Mingyan; Chen, Mary; Bhat, Indira; Ma, Linda; Haskett, Robert; Kasper, David L.; Hancock, James W.; Bhat, T. N. S.; Liang, Mingyan; Li, Lina

CORPORATE SOURCE: Department of Surgery and James H. Brown Laboratory of Immunology, University of Pittsburgh Medical Center, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: Journal of Immunology (2002), 169(6), 3382-3391  
ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Bone marrow-derived **dendritic cells** (DCs) can be genetically engineered using adenoviral (Ad) vectors to express immunosuppressive mols. that promote T cell unresponsiveness. The success of these DCs for therapy of allograft rejection has been limited in part by the potential of the adenovirus to promote DC maturation and the inherent ability of the DC to undergo maturation following in vivo administration. DC maturation occurs via NF- $\kappa$ .

B-dependent mechanisms, which can be blocked by double-stranded "decoy" oligodeoxynucleotides (ODNs) that bind

sites to NF- $\kappa$ . Berman, J.

decoy ODNs that block NF- $\kappa$ .

cells engineered to express CTLA-4-Ig or CTLA-4-Ig generate stably induced T cell unresponsiveness and potent costimulation blocking agent. The use of CTLA-4-transfected DCs exhibit markedly impaired antigen-presenting ability and promote apoptosis of activated T cells. Furthermore, administration of Ad CTLA4-Ig ODN-treated donor DCs (C57BL/10; B6 (H-2b)), heterotransplant significantly prolongs MHC-mismatched (F1H2b) C57BL/6 heart allograft survival, with long-term (400 days) donor-specific graft survival in 40% of recipients. The mechanisms responsible for DC tolerance-induction, which may involve activation-induced apoptosis of all reactive T cells, do not lead to slowing of intragraft inflammatory response. Use of NF- $\kappa$ .

**kappa.B** antisense decoys in conjunction with rAd encoding a potent costimulation blocking agent offers promise for therapy of allograft rejection or autoimmune disease with minimal or no systemic immunosuppression.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS REFERENCE. ALL CITATIONS AVAILABLE IN THE REFERENCE

136 ANSWER 1 OF 7 MARION COPYRIGHT 2002 A.A.I.M.

ACCESSION NUMBER: 2002:712316 CAPLUS

DOCUMENT NUMBER: 136

TITLE: Marked prolongation of cardiac allograft survival by **dendritic cells** genetically engineered with NF- $\kappa$ .

AUTHOR(S): Berman, J. Andrew; Bhat, Indira; Liang, Mingyan; Chen, Mary; Bhat, Indira; Ma, Linda; Haskett, Robert; Kasper, David L.; Hancock, James W.; Bhat, T. N. S.; Liang, Mingyan; Li, Lina

CORPORATE SOURCE: Department of Surgery, James H. Brown Laboratory of Immunology, University of Pittsburgh Medical Center, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: Journal of Immunology (2002), 169(6), 3382-3391  
ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

Type 1 IFN is produced by different subsets of the immune response, including a cell-mediated immunity. We have recently shown that the infection of dendritic cells with Myxoma virus interferes with IFN- $\beta$  and IFN- $\alpha$ . In this work we have monitored a rapid induction of IFN- $\beta$ , followed by the delayed prodn. of the IFN- $\alpha$  and IFN- $\gamma$ . The Mtb infection rapidly activates the NF- $\kappa$ B complex and stimulates the phosphorylation of IFN regulatory factor (IRF)-3, events known to induce IFN- $\beta$  expression in viral infection. In turn, the autocrine prodn. of IFN- $\beta$  induces the IFN-stimulated genes that contain binding sites for activated STATs in their promoters. Among the IFN-stimulated genes induced in DC through STAT activation are IRF-1 and IRF-7. The expression of IRF-1 appears to be dependent on the sequential activation of NF- $\kappa$ B and STAT-1. Once expressed, IRF-1 may further stimulate the transcription of IFN- $\beta$ . Induction of IRF-7 is also regulated at the transcriptional level through the binding of phosphorylated STAT-1 and STAT-2, forming the IFN-stimulated gene factor complex. In turn, the IRF-1 and IRF-7 expression appears to be required for the delayed induction of the IFN- $\alpha$ 1/2 prodn. Although correlative, our results strongly support the existence of a cascade of mol. events in Mtb-infected DC. Upon infection, dendritic cells express NF- $\kappa$ B. B and IRF-1 are induced and likely contribute to the rapid IFN- $\beta$  expression. In turn, IFN- $\beta$ -induced IRF-1 and IRF-7 may cooperate with induction of IFN- $\alpha$ 1/3 if infection persists and these factors are activated.

THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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2001:816672 CARLUS

135:355016

The use of tolerogenic dendritic cells for enhancing tolerogenicity is a host and methods for making the same.

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[illegible]

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[illegible]

To illustrate the effect of the dendritic compartment, dendritic cells were cultured in the presence of the  $\alpha$ - $\beta$ 1 integrin antibody, and the effect of the antibody on the expression of the  $\alpha$ - $\beta$ 1 integrin was determined. The results showed that the  $\alpha$ - $\beta$ 1 integrin antibody had no effect on the expression of the  $\alpha$ - $\beta$ 1 integrin in dendritic cells.



also, the present invention provides a method for increasing the tolerogenicity in hosts comprising administering the tolerogenic mammalian DCs of the present invention to the host. The tolerogenic DCs of the present invention comprise an oligodeoxyribonucleotide (ODN) which has one or more NF- $\kappa$ B binding sites. The tolerogenic DCs of the present invention may further comprise a viral vector, and preferably an adenoviral vector, which does not affect the tolerogenicity of the tolerogenic DCs of the present invention. Enhanced tolerogenicity in host is achieved by increasing the survival of the tolerogenic DCs in the host and by inducing tolerance in the host.

136  
 ACCESSION NUMBER: 136  
 DOCUMENT NUMBER: 136  
 TITLE: Induction of cardiac allograft survival using dendritic cells treated with NF- $\kappa$ B decoy oligodeoxyribonucleotides  
 AUTHOR(S): Giannoukakis, Nick; Bonham, C. Andrew; Qian, Shiguang; Zhou, Zhongyou; Peng, Liansha; Harnaha, Jo; Li, Wei; Inokson, Angus W.; Fung, John J.; Robbins, Paul D.; Lu, Lina  
 CORPORATE SOURCE: Department of Molecular Genetics and Biochemistry, University of Pittsburgh, Pittsburgh, PA, 15261, USA  
 SOURCE: Molecular Therapy (2000), 1(1), Pt. 1, 430-437  
 CODEN: MTHOCK; ISSN: 1525-0016  
 PUBLISHER: Academic Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Dendritic cells (DC) are highly potent in inducing a response in naive T cells. DCs are known to express a variety of costimulatory molecules (CD40, CD80, CD86) and to produce cytokines. Their capacity to induce a response in naive T cells is associated with NF- $\kappa$ B-dependent transcription of their genes. Tolerogenicity has been associated with impaired NF- $\kappa$ B-dependent transcription of costimulatory genes as well as NF- $\kappa$ B translocation to the nucleus. In this report, we demonstrate that double-stranded oligodeoxyribonucleotides (ODNs) binding sites for NF- $\kappa$ B (NF- $\kappa$ B ODN) are efficiently incorporated by bone marrow-derived DC and specifically inhibit NF- $\kappa$ B-dependent transcription of a reporter gene. Moreover, exposure of DC to the oligonucleotide decoys inhibited lipid lysosomal acid phosphatase (LAP) activity, a marker of DC maturation. Treatment of bone marrow-derived DC progenitors with NF- $\kappa$ B ODN selectively suppressed the cell surface expression of costimulatory molecules. Interfering with NF- $\kappa$ B signaling in DCs also inhibited the expression of NF- $\kappa$ B ODN. In this report, we show that the expression of NF- $\kappa$ B ODN in DCs is sufficient to induce tolerance in a murine model of cardiac allograft survival. Finally, infusion of NF- $\kappa$ B ODN into the heart of a murine model of cardiac allograft survival significantly improved graft survival. In this model, the expression of NF- $\kappa$ B ODN in DCs is sufficient to induce tolerance in a murine model of cardiac allograft survival. In this model, the expression of NF- $\kappa$ B ODN in DCs is sufficient to induce tolerance in a murine model of cardiac allograft survival. In this model, the expression of NF- $\kappa$ B ODN in DCs is sufficient to induce tolerance in a murine model of cardiac allograft survival.

REFERENCE CITED: 14  
 THERE ARE 14 OTHER REFERENCES AVAILABLE FOR THIS ENTRY. ALL CITATIONS AVAILABLE IN THE FULL-TEXT



LANGUAGE: English

AB

Molecular endothelial growth factor VEGF, produced by almost all tumor cells, affects the ability of bone marrow-derived precursor cells (BMDP) to differentiate into functional dendritic cells (DC) during the early stages of their maturation. In this study we demonstrate specific binding of VEGF to Flt-1. This binding was efficiently competed by placenta growth factor (PlGF), a ligand reportedly specific to the Flt-1 receptor. The number of binding sites for VEGF increased during DC maturation in vitro and was, with decreased levels of mRNA for Flt-1. VEGF significantly inhibited expression of NF- $\kappa$ B (NF- $\kappa$ B - expression of VEGF in the presence of Flt-1 transcripts) and of the inducible cytokines. The presence of VEGF significantly reduced the dendritic DC binding of NF- $\kappa$ B. NF- $\kappa$ B is a key transcription factor involved with NF- $\kappa$ B. The expression of NF- $\kappa$ B is blocked by decreases in the mRNA for Flt-1 and, therefore, the inhibition of NF- $\kappa$ B.

B. Effect of NF- $\kappa$ B on VEGF binding in HPC at early stages of differentiation with an adenovirus expressing a dominant NF- $\kappa$ B inhibitor or NF- $\kappa$ B. B reproduced the pattern of effects obsd. with VEGF. Thus, NF- $\kappa$ B plays an important role in maturation of HPCs to DC, and VEGF activation of the Flt-1 receptor is able to block the activation of NF- $\kappa$ B in this system. Blockade of NF- $\kappa$ B activation in HPCs by tumor-derived factors may therefore be a mechanism by which tumor cells can directly down-modulate the ability of the immune system to generate effective antitumor immune responses.

L36 ANSWER 7 OF 9 "HELIX" CONFIDENTIAL 11 11 AGO

ACCESSION NUMBER: 1947:670123

DOCUMENT NUMBER: 130,271,13

TITLE: NF-kappa

Borghese, Carlo; Di-Lo, Antonio;  
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SOURCE: (1994), 9(2), 315-323

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FOR THE FIRST TIME

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors analyzed the expression of an IL-12 receptor by fresh dendritic cells (DC) and a DC line. Using RT-PCR, RFLP protection, and electrophoretic mobility shift assay (EMSA), they found that DC possess an IL-12 receptor with identical binding characteristics as IL-1-related differences from that of T cells. IL-12 signaling through this receptor involves members of the NF- $\kappa$ B pathway, but not STAT family. The major promoter of the IL-12 receptor  $\alpha$ 1, therefore, contains several binding sites for NF- $\kappa$ B transcription factors, including IRB-1, IRF-1, IRF-3, IRF-9, IRF-7, IRF-8, IRF-10, IRF-11, IRF-12, IRF-13, IRF-14, IRF-15, IRF-16, IRF-17, IRF-18, IRF-19, IRF-20, IRF-21, IRF-22, IRF-23, IRF-24, IRF-25, IRF-26, IRF-27, IRF-28, IRF-29, IRF-30, IRF-31, IRF-32, IRF-33, IRF-34, IRF-35, IRF-36, IRF-37, IRF-38, IRF-39, IRF-40, IRF-41, IRF-42, IRF-43, IRF-44, IRF-45, IRF-46, IRF-47, IRF-48, IRF-49, IRF-50, IRF-51, IRF-52, IRF-53, IRF-54, IRF-55, IRF-56, IRF-57, IRF-58, IRF-59, IRF-60, IRF-61, IRF-62, IRF-63, IRF-64, IRF-65, IRF-66, IRF-67, IRF-68, IRF-69, IRF-70, IRF-71, IRF-72, IRF-73, IRF-74, IRF-75, IRF-76, IRF-77, IRF-78, IRF-79, IRF-80, IRF-81, IRF-82, IRF-83, IRF-84, IRF-85, IRF-86, IRF-87, IRF-88, IRF-89, IRF-90, IRF-91, IRF-92, IRF-93, IRF-94, IRF-95, IRF-96, IRF-97, IRF-98, IRF-99, IRF-100, IRF-101, IRF-102, IRF-103, IRF-104, IRF-105, IRF-106, IRF-107, IRF-108, IRF-109, IRF-110, IRF-111, IRF-112, IRF-113, IRF-114, IRF-115, IRF-116, IRF-117, IRF-118, IRF-119, IRF-120, IRF-121, IRF-122, IRF-123, IRF-124, IRF-125, IRF-126, IRF-127, IRF-128, IRF-129, IRF-130, IRF-131, IRF-132, IRF-133, IRF-134, IRF-135, IRF-136, IRF-137, IRF-138, IRF-139, IRF-140, IRF-141, IRF-142, IRF-143, IRF-144, IRF-145, IRF-146, IRF-147, IRF-148, IRF-149, IRF-150, IRF-151, IRF-152, IRF-153, IRF-154, IRF-155, IRF-156, IRF-157, IRF-158, IRF-159, IRF-160, IRF-161, IRF-162, IRF-163, IRF-164, IRF-165, IRF-166, IRF-167, IRF-168, IRF-169, IRF-170, IRF-171, IRF-172, IRF-173, IRF-174, IRF-175, IRF-176, IRF-177, IRF-178, IRF-179, IRF-180, IRF-181, IRF-182, IRF-183, IRF-184, IRF-185, IRF-186, IRF-187, IRF-188, IRF-189, IRF-190, IRF-191, IRF-192, IRF-193, IRF-194, IRF-195, IRF-196, IRF-197, IRF-198, IRF-199, IRF-200, IRF-201, IRF-202, IRF-203, IRF-204, IRF-205, IRF-206, IRF-207, IRF-208, IRF-209, IRF-210, IRF-211, IRF-212, IRF-213, IRF-214, IRF-215, IRF-216, IRF-217, IRF-218, IRF-219, IRF-220, 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Table 1. *Salmonella* serotypes and their associated diseases. *Salmonella* serotypes are classified into four groups: *S. flexneri*, *S. flexneri*, *S. flexneri*, and *S. flexneri*. The table lists the serotypes and their associated diseases.

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 110. *Environ. Biol. Fish.* 2106, 189: 1-12.  
 111. *Environ. Biol. Fish.* 2107, 190: 1-12.<

11. *Journal of the American Statistical Association*, 1977, 72, 1, 1-10.

[illegible]





FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE' ENTERED AT 11:34:16 ON 21 NOV 2002

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L6 77082 ANTISENS?  
L7 622 L1 AND L6  
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L9 1054 L2 AND L6  
L10 3 L9 AND L3  
L11 1 L11 REM L1 (11 DUPLICATES REMOVED)  
L12 18 L1 AND L11 AND L1  
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L14 1 L1 AND L11 AND L1  
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FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE' ENTERED AT 11:49:58 ON 21 NOV 2002

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L5 6 DUP REM L24 (4 DUPLICATES REMOVED)  
L6 0 L16 AND L3 AND L1  
L7 0 L16 AND L3 AND L2

119 ANNOTATED BIBLIOGRAPHY OF BIOLOGICAL ABSTRACTS INC. DUPLICATE

ACCESSION NUMBER: 119  
DOCUMENT NUMBER: 119  
TITLE: Enhancement of IRAK, p38 and NF-kappaB signal transduction in regulation of TLR2, TLR4 and TLR9 gene expression induced by lipopolysaccharide in mouse **dendritic cells**.

AUTHOR(S): An, Huachang; Yu, Yinhai; Zhang, Minghui; Xu, Hongmei; Qi, Runzi; Yan, Xiaoyi; Liu, Shuxun; Wang, Wenyu; Guo, Zhenghong; Guo, Jun; Qin, Zhihai; Cao, Xuetao (1)

CORPORATE SOURCE: (1) Institute of Immunology, Second Military Medical University, 800 Xiangyin Road, Shanghai, 20043; caoxt@public3.sta.net.cn China

SOURCE: Immunology, (May, 2002) Vol. 106, No. 1, pp. 34-45.  
<http://www.blackwell-science.com/cgi/doi/10.1046/j.1365-2567.2002.01411.x>  
ISSN: 0014-2975.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Toll-like receptors (TLRs) are evolutionarily conserved capable of recognizing pathogen-associated molecular patterns (PAMP) such as lipopolysaccharide (LPS) and CpG-containing **oligonucleotides** (CpG ODN). TLR2 and TLR4 are major receptors for Gram-positive and Gram-negative bacterial cell wall components, respectively. TLR9 is necessary for CpG signalling. LPS or CpG ODN can activate immature **dendritic cells** (DC) and induce DC maturation characterized by production of cytokines, up-regulation of co-stimulatory molecules, and increased ability to activate T cells. However, little is known regarding the regulation of TLR gene expression in mouse DC. In this study, we investigated the regulation of TLR2, TLR4 and TLR9 gene expression by LPS in murine immature DC. TLR2, TLR4 and TLR9 mRNA were up-regulated following LPS stimulation. The up-regulation of TLR9 expression coincided with significantly increased production of tumour necrosis factor-alpha induced by LPS plus CpG ODN. While inhibition of extracellular signal-related kinase and NF-kappaB activation suppressed the up-regulation of the expression of TLR2, TLR4 and TLR9 mRNA, inhibition of p38 kinase prevented the up-regulation of TLR2 and TLR4 mRNA expression but enhanced the up-regulation of TLR9 expression. These results demonstrate that TLR2, TLR4 and TLR9 gene expression was up-regulated by LPS in immature DC. Up-regulation of TLR2, TLR4 and TLR9 expression by LPS may promote the overall response of DC to bacterial infection to explain the synergy between LPS and other bacterial products in the induction of cytokine production.

119 ANNOTATED BIBLIOGRAPHY OF BIOLOGICAL ABSTRACTS INC. DUPLICATE

ACCESSION NUMBER: 119  
DOCUMENT NUMBER: 119  
TITLE: Expression of different NFkappa-B pathway genes in **dendritic cells** (DC) or macrophages assessed by gene expression profiling.

AUTHOR(S): Paltathakis, Ioannis (1); Alcantara, Orlando (1); Boldt, David H. (1)

CORPORATE SOURCE: (1) Medicine-Hematology, University of Texas Health Science Center, San Antonio, TX USA

SOURCE: Blood, November 14, 2001 Vol. 98, No. 11 Part 1, pp. 311a. print.

Abstract in: Blood, November 14, 2001 Vol. 98, No. 11 Part 1, pp. 311a. print.  
Abstract in: Blood, November 14, 2001 Vol. 98, No. 11 Part 1, pp. 311a. print.

Abstract in: Blood, November 14, 2001 Vol. 98, No. 11 Part 1, pp. 311a. print.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY (Abstract):





REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PATENT INFORMATION 11

[illegible]

PATENT INFORMATION:

CONCLUSIONS: The results of this study suggest that the use of a single, standardized, and validated questionnaire can be used to assess the prevalence of the most common types of musculoskeletal disorders in the workplace.

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CG, CI, CN, GA, GN, GE, HL, HR, NE, OI, TL, TG

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W:	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AV	AW	AX	AY	AZ	BA	BB	BC	BD	BE	BF	BG	BH	BI	BJ	BK	BL	BM	BN	BO	BP	BQ	BR	BS	BT	BV	BW	BX	BY	BZ	CA	CB	CC	CD	CE	CF	CG	CH	CI	CJ	CK	CL	CM	CN	CO	CP	CQ	CR	CS	CT	CU	CV	CW	CX	CY	CZ	DA	DB	DC	DD	DE	DF	DG	DH	DI	DJ	DK	DL	DM	DN	DO	DP	DQ	DR	DS	DT	DU	DV	DW	DX	DY	DZ	EA	EB	EC	ED	EE	EF	EG	EH	EI	EJ	EK	EL	EM	EN	EO	EP	EQ	ER	ES	ET	EU	EV	EW	EX	EY	EZ	FA	FB	FC	FD	FE	FF	FG	FH	FI	FJ	FK	FL	FM	FN	FO	FP	FQ	FR	FS	FT	FU	FV	FW	FX	FY	FZ	GA	GB	GC	GD	GE	GF	GG	GH	GI	GJ	GK	GL	GM	GN	GO	GP	GQ	GR	GS	GT	GU	GV	GW	GX	GY	GZ	HA	HB	HC	HD	HE	HF	HG	HH	HI	HJ	HK	HL	HM	HN	HO	HP	HQ	HR	HS	HT	HU	HV	HW	HX	HY	HZ	IA	IB	IC	ID	IE	IF	IG	IH	II	IJ	IK	IL	IM	IN	IO	IP	IQ	IR	IS	IT	IU	IV	IW	IX	IY	IZ	JA	JB	JC	JD	JE	JF	JG	JH	JI	JJ	JK	JL	JM	JN	JO	JP	JQ	JR	JS	JT	JU	JV	JW	JX	JY	JZ	KA	KB	KC	KD	KE	KF	KG	KH	KI	KJ	KK	KL	KM	KN	KO	KP	KQ	KR	KS	KT	KU	KV	KW	KX	KY	KZ	LA	LB	LC	LD	LE	LF	LG	LH	LI	LJ	LK	LL	LM	LN	LO	LP	LQ	LR	LS	LT	LU	LV	LW	LX	LY	LZ	MA	MB	MC	MD	ME	MF	MG	MH	MI	MJ	MK	ML	MM	MN	MO	MP	MQ	MR	MS	MT	MU	MV	MW	MX	MY	MZ	NA	NB	NC	ND	NE	NF	NG	NH	NI	NJ	NK	NL	NM	NN	NO	NP	NQ	NR	NS	NT	NU	NV	NW	NX	NY	NZ	OA	OB	OC	OD	OE	OF	OG	OH	OI	OJ	OK	OL	OM	ON	OO	OP	OQ	OR	OS	OT	OU	OV	OW	OX	OY	OZ	PA	PB	PC	PD	PE	PF	PG	PH	PI	PJ	PK	PL	PM	PN	PO	PP	PQ	PR	PS	PT	PU	PV	PW	PX	PY	PZ	QA	QB	QC	QD	QE	QF	QG	QH	QI	QJ	QK	QL	QM	QN	QO	QP	QQ	QR	QS	QT	QU	QV	QW	QX	QY	QZ	RA	RB	RC	RD	RE	RF	RG	RH	RI	RJ	RK	RL	RM	RN	RO	RP	RQ	RR	RS	RT	RU	RV	RW	RX	RY	RZ	SA	SB	SC	SD	SE	SF	SG	SH	SI	SJ	SK	SL	SM	SN	SO	SP	SQ	SR	SS	ST	SU	SV	SW	SX	SY	SZ	TA	TB	TC	TD	TE	TF	TG	TH	TI	TJ	TK	TL	TM	TN	TO	TP	TQ	TR	TS	TT	TU	TV	TW	TX	TY	TZ	UA	UB	UC	UD	UE	UF	UG	UH	UI	UJ	UK	UL	UM	UN	UO	UP	UQ	UR	US	UT	UU	UV	UW	UX	UY	UZ	VA	VB	VC	VD	VE	VF	VG	VH	VI	VJ	VK	VL	VM	VN	VO	VP	VQ	VR	VS	VT	VU	VV	VW	VX	VY	VZ	WA	WB	WC	WD	WE	WF	WG	WH	WI	WJ	WK	WL	WM	WN	WO	WP	WQ	WR	WS	WT	WU	WV	WW	WX	WY	WZ	XA	XB	XC	XD	XE	XF	XG	XH	XI	XJ	XK	XL	XM	XN	XO	XP	XQ	XR	XS	XT	XU	XV	XW	XX	XY	XZ	YA	YB	YC	YD	YE	YF	YG	YH	YI	YJ	YK	YL	YM	YN	YO	YP	YQ	YR	YS	YT	YU	YV	YW	YX	YY	YZ	ZA	ZB	ZC	ZD	ZE	ZF	ZG	ZH	ZI	ZJ	ZK	ZL	ZM	ZN	ZO	ZP	ZQ	ZR	ZS	ZT	ZU	ZV	ZW	ZX	ZY	ZZ
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01	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO
02	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY	AZ	BA	BB	BC	BD
03	BE	BF	BG	BH	BI	BJ	BK	BL	BM	BN	BO	BP	BQ	BR	BS
04	BT	BU	BV	BW	BX	BY	BZ	CA	CB	CC	CD	CE	CF	CG	CH
05	CI	CJ	CK	CL	CM	CN	CO	CP	CQ	CR	CS	CT	CU	CV	CW
06	CX	CY	CZ	DA	DB	DC	DD	DE	DF	DG	DH	DI	DJ	DK	DL
07	DM	DN	DO	DP	DQ	DR	DS	DT	DU	DV	DW	DX	DY	DZ	EA
08	EB	EC	ED	EE	EF	EG	EH	EI	EJ	EK	EL	EM	EN	EO	EP
09	EQ	ER	ES	ET	EU	EV	EW	EX	EY	EZ	FA	FB	FC	FD	FE
10	FF	FG	FH	FI	FJ	FK	FL	FM	FN	FO	FP	FQ	FR	FS	FT

[illegible]

W	AE	AG	AL	AM	AN	AO	AP	AR	AS	AT	AW	AX	AY	AZ	BA	BB	BC	BD	BE	BF	BG	BH	BI	BJ	BK	BL	BM	BN	BO	BP	BQ	BR	BS	BT	BV	BW	BX	BY	BZ	CA	CB	CC	CD	CE	CF	CG	CH	CI	CJ	CK	CL	CM	CN	CO	CP	CQ	CR	CS	CT	CU	CV	CW	CX	CY	CZ	DA	DB	DC	DD	DE	DF	DG	DH	DI	DJ	DK	DL	DM	DN	DO	DP	DQ	DR	DS	DT	DU	DV	DW	DX	DY	DZ	EA	EB	EC	ED	EE	EF	EG	EH	EI	EJ	EK	EL	EM	EN	EO	EP	EQ	ER	ES	ET	EU	EV	EW	EX	EY	EZ	FA	FB	FC	FD	FE	FF	FG	FH	FI	FJ	FK	FL	FM	FN	FO	FP	FQ	FR	FS	FT	FU	FV	FW	FX	FY	FZ	GA	GB	GC	GD	GE	GF	GG	GH	GI	GJ	GK	GL	GM	GN	GO	GP	GQ	GR	GS	GT	GU	GV	GW	GX	GY	GZ	HA	HB	HC	HD	HE	HF	HG	HH	HI	HJ	HK	HL	HM	HN	HO	HP	HQ	HR	HS	HT	HU	HV	HW	HX	HY	HZ	IA	IB	IC	ID	IE	IF	IG	IH	II	IJ	IK	IL	IM	IN	IO	IP	IQ	IR	IS	IT	IU	IV	IW	IX	IY	IZ	JA	JB	JC	JD	JE	JF	JG	JH	JI	JJ	JK	JL	JM	JN	JO	JP	JQ	JR	JS	JT	JU	JV	JW	JX	JY	JZ	KA	KB	KC	KD	KE	KF	KG	KH	KI	KJ	KK	KL	KM	KN	KO	KP	KQ	KR	KS	KT	KU	KV	KW	KX	KY	KZ	LA	LB	LC	LD	LE	LF	LG	LH	LI	LJ	LK	LM	LN	LO	LP	LQ	LR	LS	LT	LU	LV	LW	LX	LY	LZ	MA	MB	MC	MD	ME	MF	MG	MH	MI	MJ	MK	ML	MM	MN	MO	MP	MQ	MR	MS	MT	MU	MV	MW	MX	MY	MZ	NA	NB	NC	ND	NE	NF	NG	NH	NI	NJ	NK	NL	NM	NO	NP	NQ	NR	NS	NT	NU	NV	NW	NX	NY	NZ	OA	OB	OC	OD	OE	OF	OG	OH	OI	OJ	OK	OL	OM	ON	OO	OP	OQ	OR	OS	OT	OU	OV	OW	OX	OY	OZ	PA	PB	PC	PD	PE	PF	PG	PH	PI	PJ	PK	PL	PM	PN	PO	PP	PQ	PR	PS	PT	PU	PV	PW	PX	PY	PZ	QA	QB	QC	QD	QE	QF	QG	QH	QI	QJ	QK	QL	QM	QN	QO	QP	QR	QS	QT	QU	QV	QW	QX	QY	QZ	RA	RB	RC	RD	RE	RF	RG	RH	RI	RJ	RK	RL	RM	RN	RO	RP	RQ	RR	RS	RT	RU	RV	RW	RX	RY	RZ	SA	SB	SC	SD	SE	SF	SG	SH	SI	SJ	SK	SL	SM	SN	SO	SP	SQ	SR	SS	ST	SU	SV	SW	SX	SY	SZ	TA	TB	TC	TD	TE	TF	TG	TH	TI	TJ	TK	TL	TM	TN	TO	TP	TQ	TR	TS	TT	TU	TV	TW	TX	TY	TZ	UA	UB	UC	UD	UE	UF	UG	UH	UI	UJ	UK	UL	UM	UN	UO	UP	UQ	UR	US	UT	UU	UV	UW	UX	UY	UZ	VA	VB	VC	VD	VE	VF	VG	VH	VI	VJ	VK	VL	VM	VN	VO	VP	VQ	VR	VS	VT	VU	VW	VX	VY	VZ	WA	WB	WC	WD	WE	WF	WG	WH	WI	WJ	WK	WL	WM	WN	WO	WP	WQ	WR	WS	WT	WU	WV	WW	WX	WY	WZ	XA	XB	XC	XD	XE	XF	XG	XH	XI	XJ	XK	XL	XM	XN	XO	XP	XQ	XR	XS	XT	XU	XV	XW	XX	XY	XZ	YA	YB	YC	YD	YE	YF	YG	YH	YI	YJ	YK	YL	YM	YN	YO	YP	YQ	YR	YS	YT	YU	YV	YW	YX	YY	YZ	ZA	ZB	ZC	ZD	ZE	ZF	ZG	ZH	ZI	ZJ	ZK	ZL	ZM	ZN	ZO	ZP	ZQ	ZR	ZS	ZT	ZU	ZV	ZW	ZX	ZY	ZZ
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PRIORITY MAIL, INC.



AB Antisense oligonucleotides, 100001, antisense oligonucleotides  
: Antisense oligonucleotides, 100001, antisense oligonucleotides  
nuclear factor-kappa B, 100001  
known to enhance T-cell growth and dendritic cell  
function. The oligos suppress cytokine levels, particularly antisense  
oligonucleotides, 100001, antisense oligonucleotides.

REFERENCE FORM: 1-1. THESE ARE THE REFERENCES AVAILABLE FOR THIS  
REF. ALL CITATIONS AVAILABLE IN THE REF. FORM

019 ANWER 6 OF 11 CAPINS COPYRIGHT 2004 ACS  
 ACCESSION NUMBER: 001:011744 CAPINS  
 DOCUMENT NUMBER: 130:4673  
 TITLE: Expression of different NF-kappa.B pathway genes in  
 dendritic cells (DCs) or macrophages  
 assessed by gene expression profiling  
 AUTHOR(S): Baltathakis, Ioannis; Alcantara, Orlando; Boldt, David  
 H.  
 CORPORATE SOURCE: Medicine/Hematology, University of Texas Health  
 Science Center, San Antonio, TX, 78229-3900, USA  
 SOURCE: Journal of Cellular Biochemistry 200411, 93(2),  
 431-437  
 WHEN: 2004; LANG: ENGLISH  
 PUBLISHER: Wiley-Liss, Inc.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English

AB NF- $\kappa$ B plays a central role in immune system regulation in the different cellular compartments, either **dendritic cells** [1]. In dendritic cells, it acts as an activator of IL6 from anti-inflammatory and pro-inflammatory cells. Recent studies of the expression pattern of Rel proteins and their inhibitors (I. $\kappa$ B $\alpha$ ) suggest that there is a critical timing in this differentiation process is transcriptional. To investigate differential gene expression between macrophages and DCs, we used a cDNA available gene microarrays (GEArray K17), which included four of the NF- $\kappa$ B/Rel family genes (*p50/p105*, *p52/p100*, *I $\kappa$ B $\alpha$* , and *I $\kappa$ B $\beta$* ), and two other genes either in the NF- $\kappa$ B signal transduction pathway or under transcriptional control of NF- $\kappa$ B/Rel factors. The dendritic macrophages and DCs, both adherent peripheral blood monocytes were cultured with IL-1 $\beta$  + IL-18 + IL-4 resp. for up to 4 days. Cells were harvested, macrophages were treated with lipopolysaccharide (LPS) and the rest left untreated. Induced matured DCs cells were harvested after 3 days. RNA was purified and radiolabeled with gamma-<sup>32</sup>P-ATP, then hybridized to Gene arrays containing specific probes for p50-p105 and I $\kappa$ B $\alpha$ . With a PhosphorImaging screen, we found that the expression of I $\kappa$ B $\alpha$  and I $\kappa$ B $\beta$  was

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT





## A5

**kappa.B** (NK-.kappa.B). Methods. Murine macrophage-like

RAW 264.7 cells were incubated with 1.0 μM LPS and pGd CpG-containing oligonucleotides (CpG ODN) for 1 h. Cells were restimulated with 1.0 μM LPS for 10 minutes. The cells were cotransfected with an NF-κappa.B signaling luciferase reporter construct and a control vector as plasmid. NF-kappa.B activation was detected by appearance of NF-κappa.B-dependent transcriptional activity using luciferase reporter system. In addition, I.kappa.B, I.kappa.B kinase and phosphorylated-I.kappa.B by Western blotting, cytosolic calcium activity, and intracellular cAMP levels were measured by fluorescence assay. Results. NF-κappa.B transcriptional activity was increased as demonstrated by luciferase activity assay in the prolonged CpG ODN pretreatment groups. Unlike endotoxin tolerance, CpG ODN pre-exposure increased cytoplasmic phospho-I.kappa.B.alpha. and did not abrogate mitogen-activated protein kinase activity. Conclusions. In macrophages, exposure to CpG DNA increases expression of the inhibitory p50 NF-κappa.B homodimer and decreases NF-κappa.P activity without inhibition of I.kappa.B kinases. Mitogen-activated protein kinase activity remains intact. Understanding these interactions between different toll receptor ligands may provide insight into novel therapeutic modalities.



AB NF- $\kappa$ B and Rel transcription factors have been implicated in the differentiation of monocytes to either dendritic cells (DCs) or macrophages, as well as in the maturation of DCs from antigen-processing to antigen-presenting cells. Recent studies of the expression pattern of Rel proteins and their inhibitors (IkappaBs), suggest that their regulation during this differentiation process is transcriptional. To investigate differential gene expression between macrophages and DCs, we used commercially available gene chip arrays (GeneChip K11), which included four of the NF- $\kappa$ B/Rel family genes (p105/p50, p50/p51, RelB, and c-Rel) and a control gene unrelated to the NF- $\kappa$ B signal transduction pathway (GAPDH) for transcriptional analysis. In DCs generated from monocytes, macrophages, and DCs, human adherent peritoneal macrophages were cultured with M-CSF or GM-CSF + IL-4 respectively for 4 to 7 days. In *in vivo* experiments, macrophages were treated with LPS (lipopolysaccharide) for the last 48 h of culture to induce maturation. Cells were harvested after 7 days, cDNA was prepared and analyzed with alpha-<sup>32</sup>P-UTP-PCR, then hybridized to gene arrays containing specific gene probes, beta-actin and GAPDH or PUC18 oligonucleotides served as positive or negative controls, respectively. The expression of all four NF- $\kappa$ B/Rel family genes examined was significantly upregulated in maturing DCs compared to macrophages. The strongest difference was observed for c-Rel. RT-PCR determinations of c-Rel, RelB, and p105 mRNAs confirmed these observations. Among the 32 NF- $\kappa$ B/Rel pathway genes, 14 were upregulated in mature DCs compared to macrophages. These genes were IkappaBalpha, IKK-beta, NIK, ICAM-1, P-selectin, E-selectin, TNF-alpha, TNFR2, TNFAIP3, IL-1alpha, IL-1R1, IL-1R2, IRAK, and TANK. By contrast, only MCP-1 (monocyte chemotactic protein 1) was upregulated in macrophages compared to DCs. NF- $\kappa$ B pathway genes upregulated in DCs compared to macrophages were constitutively expressed in monocytes then selectively downregulated during macrophage but not DC differentiation. LPS did not induce expression of most of these genes in macrophages but LPS did induce upregulation of some of these genes in DCs. We conclude that NF- $\kappa$ B/Rel family genes, including NIK, are constitutively expressed in DCs; downregulated in macrophages; and upregulated in DCs. However, this differential expression is not correlated with activation of different NF- $\kappa$ B signal transduction pathways in DCs and macrophages and with expression of a unique subset of genes in LPS that are transcriptionally targeted by NF- $\kappa$ B/Rel factors. The results illustrate the ability of the NF- $\kappa$ B pathway to respond to differentiation stimuli by activating in a cell-specific manner unique signaling pathways and subsets of NF- $\kappa$ B target genes.

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L21 ANSWER: 106.75

Figure 1. A schematic diagram of the experimental design. The subjects were divided into two groups: the control group and the experimental group. The control group received a standard 12-week training program, while the experimental group received a modified 12-week training program. The modified program included a 4-week pre-training period followed by an 8-week training period. The subjects were then divided into two subgroups: the control subgroup and the experimental subgroup. The control subgroup received a standard 12-week training program, while the experimental subgroup received a modified 12-week training program. The subjects were then divided into two subgroups: the control subgroup and the experimental subgroup. The control subgroup received a standard 12-week training program, while the experimental subgroup received a modified 12-week training program.

1. The first step is to identify the key components of the system. This includes understanding the hardware, software, and data involved.

1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	2127	2128	2129	2130	2131	2132	2133	2134	2135	2136	2137	2138	2139	2140	2141	2142	2143	2144	2145	2146	2147	2148	2149	2150	2151	2152	2153	2154	2155	2156	2157	2158	2159	2160	2161	2162	2163	2164	2165	2166	2167	2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	2183	2184	2185	2186	2187	2188	2189	2190	2191	2192	2193	2194	2195	2196	2197	2198	2199	2200	2201	2202	2203	2204	2205	2206	2207	2208	2209	2210	2211	2212	2213	2214	2215	2216	2217	2218	2219	2220	2221	2222	2223	2224	2225	2226	2227	2228	2229	2230	2231	2232	2233	2234	2235	2236	2237	2238	2239	2240	2241	2242	2243	2244	2245	2246	2247	2248	2249	2250	2251	2252	2253	2254	2255	2256	2257	2258	2259	2260	2261	2262	2263	2264	2265	2266	2267	2268	2269	2270	2271	2272	2273	2274	2275	2276	2277	2278	2279	2280	2281	2282	2283	2284	2285	2286	2287	2288	2289	2290	2291	2292	2293	2294	2295	2296	2297	2298	2299	2300	2301	2302	2303	2304	2305	2306	2307	2308	2309	2310	2311	2312	2313	2314	2315	2316	2317	2318	2319	2320	2321	2322	2323	2324	2325	2326	2327	2328	2329	2330	2331	2332	2333	2334	2335	2336	2337	2338	2339	2340	2341	2342	2343	2344	2345	2346	2347	2348	2349	2350	2351	2352	2353	2354	2355	2356	2357	2358	2359	2360	2361	2362	2363	2364	2365	2366	2367	2368	2369	2370	2371	2372	2373	2374	2375	2376	2377	2378	2379	2380	2381	2382	2383	2384	2385	2386	2387	2388	2389	2390	2391	2392	2393	2394	2395	2396	2397	2398</
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AB C1b, block signaling, and phagocytosis, and stimulate leukocyte surface glycoprotein, membrane leukocyte adhesion and transmit activating signals in T cells and dendritic cells. Immunized anti-C1b monoclonal antibody (mAb) MPM-1 has been previously shown to induce apoptosis of dendritic cells *in vitro*. In this study we show that it also triggers apoptosis of the myeloid dendritic cell line TF-1. The kinetics of the MPM-1-induced apoptosis were analyzed along with the first apoptotic cell appearance and the cell cycle distribution of the immunized dendritic cells. The results show that MPM-1-mediated apoptosis occurs in a dose-dependent manner. The

polyclonal anti-CD43 mAb (anti-CD43 (MEM-3) or anti-CD99 mAb. The MEM-3-mediated apoptosis of TF-1 cells was also inhibited by the overexpression of a specific inhibitor, Baxx. CD43-mediated apoptosis was preceded by the repression of the DNA binding activity of the transcription factor NF- $\kappa$ B. RNA array screening revealed that the expression of several genes encoding apoptosis-regulating proteins, including 14-3-3 proteins and the granulocyte macrophage colony-stimulating factor (GM-CSF) receptor beta-subunit, was repressed in TF-1 cells bound to immobilized MEM-39. The down-regulation of 14-3-3 proteins and GM-CSF receptor beta was accompanied by translocation of the proapoptotic protein Bad to the mitochondria. These results suggest that engagement of CD43 may, presumably through the repressing transcription, initiate a Bad-dependent apoptotic pathway.

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L21 ANSWER 5 OF 17          UNLBI)
ADDRESS: L1 UNLBI)
DOCUMENT NUMBER:            UNLBI)
TITLE:                      + Toll-like receptor 1 binds to lipote wall-bein; via
                             + toll-like receptor 1-likereceptor TOLL-like receptor
AUTHOR:                     Jansen Geoffrey B; Brunn Gregory J; Kodaira Yuzo; Platt
                             Jeffrey L
CORPORATE SOURCE:           Department of Immunology, Mayo Clinic, 2-66 Medical
                             Sciences Building, Rochester, MN 55905, USA.
CONTRACT NUMBER:           HL 4-01 UNLBI)
                             H' 52297 UNLBI)
SOURCE:                     JOURNAL OF IMMUNOLOGY, (2002 May 15) 168 (10) 5233-9.
                             Journal code: 2985117X. ISSN: 0022-1767.
PUB. COUNTRY:              United States
DOCUMENT TYPE:              Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:                   English
FILE SEGMENT:               Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:                200205
ENTRY DATE:                 Entered UNTN: 10 2002-
                             Last Updated on UNTN: 10 2002-
                             Deleted On UNTN: 10 2002-
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AB In addition to the well characterized T cell-like pattern and interactions, dendritic cells generate responses to a wide range of stimuli that are recognized by innate immune receptors. Dendritic cells have a major role in capturing or specialized cells such as **dendritic cells**, for which the nature of the receptors responsible for fragments of cell surface molecules is not known. We found that the T cell-like receptor of a **dendritic cells** might be a cell-surface glycoprotein fragments of heparan sulfate polysaccharide. **Dendritic cells** were found to mature in response to heparan sulfate as measured by a stimulatory protein expression, CD86, CD80, and T lymphocyte activation, but this maturation was absent when T cell-like receptor 4 was mutated or inhibited. These findings suggest that T cell-like receptors in vertebrates may monitor tissue well-being by recognizing fragments of endogenous macromolecules.

[illegible]

**CONCLUSIONS** The results of this study suggest that the use of a single, low-dose, intravenous bolus of propofol may be sufficient to achieve adequate sedation for the majority of patients undergoing colonoscopy. However, additional doses may be required during the procedure. The use of propofol for conscious sedation in the ambulatory setting appears to be safe and effective.

LANGSTON :  
FILE # 100000:  
ENTRY NAME:  
ENTRY DATE:

AB Dendritic cells (DC) constitute a complex system of uniquely well-equipped antigen-presenting cells that initiate and regulate immune responses. Extensive recent studies have improved our understanding of DC development, differentiation, activation, and function. DC exist as distinct subsets that differ in their lineage, activation, surface molecule expression, and biological function. These factors serve to determine the T-cell polarizing signals and type of T cell response--T helper 1, T helper 2, or T regulatory--induced by DC [1]. Evidence has accumulated that DC play an important role in both central and peripheral tolerance via various mechanisms, including induction of T-cell anergy, immune deviation, T-regulatory cell activity, and promotion of activated T-cell apoptosis. With many of the details of the molecular basis of DC tolerance still unknown, the emerging information suggests that control of the DC phenotype, including expression of death-inducing ligands, is particularly important. Thus, local, micro-environmental factors (in particular, anti-inflammatory immunosuppressive cytokines), and inhibition of gene transcription of regulatory proteins (e.g., nuclear factor-kappaB) can impact tolerogenic potential of DC [2]. Manipulation of DC by control of their maturation and differentiation, or genetic engineering of these cells to express immunosuppressive molecules, offers potential for therapy of allograft rejection and autoimmune disease. In this brief overview, we outline principles and methods for generation of "tolerogenic" DC and outcomes that have been reported in experimental models. Space constraints limit literature citations.

L21 ANSWER 7 OF 15 MEDLINE  
 ACCESSION NUMBER: 2002171821 MEDLINE  
 DOCUMENT NUMBER: 219000695 PubMed ID: 11907895  
 TITLE: RNA array and biological characterization of the impact  
 of the maternal status of the **dendritic  
 cells** on the progeny type and duration of gestation  
 in mice.  
 AUTHOR: Gaudet D; Gaudet D; Gaudet D; Gaudet D; Gaudet D; Gaudet D;  
 Gaudet D; Gaudet D  
 CORPORATE AUTHOR: Universite du Quebec, Centre, Trois-Rivieres, Quebec, Canada,  
 Trois-Rivieres, Quebec, Canada, J1N 4B5, Canada.  
 SOURCE: MEDLINE (INDEX) 14, 11, 11 Nov 2002 14:11:00-01.  
 URL: http://www.ncbi.nlm.nih.gov/pubmed/11907895  
 PUB. C. DIFF.  
 DOCUMENT TYPE: Journal Article; Research Support  
 LANGUAGE: English  
 FILE OR IDENT: 11907895  
 ENTRY MONTH: 11/01  
 ENTRY DATE: 2002171821  
 Last Updated on STD: 11/01/02  
 Entered on STD: 11/01/02

AB We systematically investigated the impact of the relative neuronal levels of **dendritic cells** (DC) on the development of the phenotype, expression of cytokines and chemokines, and the ability to phagocytose and kill bacteria. We found that the ability to phagocytose and kill bacteria was significantly reduced in mice with low levels of DC. These results suggest that DC are important for the development of the phenotype and the ability to phagocytose and kill bacteria.

[illegible]

121 ANSWER - OF 1 - ABSTRACTS  
ACCESSION NUMBER: 2001:049019 CAPLOS  
DOCUMENT NUMBER: 1301153756  
TITLE: Potential role of phosphatidylinositol 3 kinase, rather than DNA-dependent protein kinase, in CpG DNA-induced immune activation.  
AUTHOR(S): Ishii, Ken J.; Takeshita, Fumihiko; Gursel, Ihsan; Gursel, Mayda; Cnover, Jacqueline; Nussenzweig, Andre; Klinman, Dennis M.  
CORPORATE SOURCE: Section of Retroviral Immunology, Division of Viral Products, Center for Biologics Evaluation and Research, Food and Drug Administration, National Institutes of Health, Bethesda, MD, 20892, USA  
SOURCE: Journal of Experimental Medicine 2001, 193(1), 139-144  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ABSTRACT: Bacterial lipopolysaccharide (LPS) and CpG DNA stimulate a strong innate immune response. There is evidence that DNA-dependent protein kinase (DNA-PK) mediates CpG signaling. Specifically, wortmannin (an inhibitor of phosphatidylinositol 3 kinase [PI3]-kinases including DNA-PK) interferes with CpG-dependent cell activation, and DNA-PK knockout (KO) mice fail to respond to CpG stimulation. Current studies establish that wortmannin actually inhibits the uptake and colocalization of CpG DNA with toll-like receptor (TLR)-9 in endosomal vesicles, thereby preventing CpG-induced activation of the NF-kappa-B signaling cascade. We find that DNA-PK is not involved in this process, since three strains of DNA-PK KO mice responded normally to CpG DNA. These results support a model in which CpG signaling is mediated through TLR-9 but not DNA-PK, and suggest that wortmannin-sensitive members of the PI3-kinase family play a critical role in controlling CpG DNA-TLR-9.

REFERENCE COUNT: 13  
THREE ARE CURRENTLY AVAILABLE FOR THIS REFERENCE. ALL MATERIAL AVAILABLE IN THE REFERENCE

[illegible]





WO 2000053756	A2	20000914	WO 2000-084341	20000914
WO 2000053756	A3	20010201		
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WO 2001016318	A	20010414		
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XY:	XA	XB	XC	XD	XE	XF	YG	YH	YI	YJ	YK	YL	YM	YN	YO	YP	YQ	YR	YS	YT	YU	YV	YW
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Wc: 21.0104040	A: 21.0104040

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RW:	GH, GN, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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EP 1240325                      NO. 00020913

[illegible]

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BN:	AB, BA, CA, CB, DA, DB, EA, EB, FA, FB, GA, GB, HA, HB, IA, IB, JA, JB, KA, KB, LA, LB, MA, MB, NA, NB, OA, OB, PA, PB, QA, QB, RA, RB, SA, SB, TA, TB, UA, UB, VA, VB, WA, WB, XA, XB, YA, YB, ZA, ZB

WC 200205823; A2 10020451

[illegible]

Case	Age	Sex	Site	Pathologic	Survival
1	50	M	Stomach	Adenocarcinoma	10 months
2	65	F	Stomach	Adenocarcinoma	12 months
3	70	M	Stomach	Adenocarcinoma	18 months
4	68	F	Stomach	Adenocarcinoma	24 months
5	72	M	Stomach	Adenocarcinoma	30 months
6	60	F	Stomach	Adenocarcinoma	36 months
7	75	M	Stomach	Adenocarcinoma	42 months
8	62	F	Stomach	Adenocarcinoma	48 months
9	78	M	Stomach	Adenocarcinoma	54 months
10	66	F	Stomach	Adenocarcinoma	60 months
11	71	M	Stomach	Adenocarcinoma	66 months
12	64	F	Stomach	Adenocarcinoma	72 months
13	73	M	Stomach	Adenocarcinoma	78 months
14	69	F	Stomach	Adenocarcinoma	84 months
15	76	M	Stomach	Adenocarcinoma	90 months
16	61	F	Stomach	Adenocarcinoma	96 months
17	74	M	Stomach	Adenocarcinoma	102 months
18	67	F	Stomach	Adenocarcinoma	108 months
19	77	M	Stomach	Adenocarcinoma	114 months
20	63	F	Stomach	Adenocarcinoma	120 months
21	79	M	Stomach	Adenocarcinoma	126 months
22	65	F	Stomach	Adenocarcinoma	132 months
23	72	M	Stomach	Adenocarcinoma	138 months
24	68	F	Stomach	Adenocarcinoma	144 months
25	75	M	Stomach	Adenocarcinoma	150 months
26	62	F	Stomach	Adenocarcinoma	156 months
27	78	M	Stomach	Adenocarcinoma	162 months
28	66	F	Stomach	Adenocarcinoma	168 months
29	71	M	Stomach	Adenocarcinoma	174 months
30	64	F	Stomach	Adenocarcinoma	180 months
31	73	M	Stomach	Adenocarcinoma	186 months
32	69	F	Stomach	Adenocarcinoma	192 months
33	76	M	Stomach	Adenocarcinoma	198 months
34	61	F	Stomach	Adenocarcinoma	204 months
35	74	M	Stomach	Adenocarcinoma	210 months
36	67	F	Stomach	Adenocarcinoma	216 months
37	77	M	Stomach	Adenocarcinoma	222 months
38	63	F	Stomach	Adenocarcinoma	228 months
39	79	M	Stomach	Adenocarcinoma	234 months
40	65	F	Stomach	Adenocarcinoma	240 months
41	72	M	Stomach	Adenocarcinoma	246 months
42	68	F	Stomach	Adenocarcinoma	252 months
43	75	M	Stomach	Adenocarcinoma	258 months
44	62	F	Stomach	Adenocarcinoma	264 months
45	78	M	Stomach	Adenocarcinoma	270 months
46	66	F	Stomach	Adenocarcinoma	276 months
47	71	M	Stomach	Adenocarcinoma	282 months
48	64	F	Stomach	Adenocarcinoma	288 months
49	73	M	Stomach	Adenocarcinoma	294 months
50	69	F	Stomach	Adenocarcinoma	300 months
51	76	M	Stomach	Adenocarcinoma	306 months
52	61	F	Stomach	Adenocarcinoma	312 months
53	74	M	Stomach	Adenocarcinoma	318 months
54	67	F	Stomach	Adenocarcinoma	324 months
55	77	M	Stomach	Adenocarcinoma	330 months
56	63	F	Stomach	Adenocarcinoma	336 months
57	79	M	Stomach	Adenocarcinoma	342 months
58	65	F	Stomach	Adenocarcinoma	348 months
59	72	M	Stomach	Adenocarcinoma	354 months
60	68	F	Stomach	Adenocarcinoma	360 months
61	75	M	Stomach	Adenocarcinoma	366 months
62	62	F	Stomach	Adenocarcinoma	372 months
63	78	M	Stomach	Adenocarcinoma	378 months
64	66	F	Stomach	Adenocarcinoma	384 months
65	71	M	Stomach	Adenocarcinoma	390 months
66	64	F	Stomach	Adenocarcinoma	396 months
67	73	M	Stomach	Adenocarcinoma	402 months
68	69	F	Stomach	Adenocarcinoma	408 months
69	76	M	Stomach	Adenocarcinoma	414 months
70	61	F	Stomach	Adenocarcinoma	420 months
71	74	M	Stomach	Adenocarcinoma	426 months
72	67	F	Stomach	Adenocarcinoma	432 months
73	77	M	Stomach	Adenocarcinoma	438 months
74	63	F	Stomach	Adenocarcinoma	444 months
75	79	M	Stomach	Adenocarcinoma	450 months
76	65	F	Stomach	Adenocarcinoma	456 months
77	72	M	Stomach	Ad	





gr. 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.

L21 ANSWER IN: 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.  
ACCESSION NUMBER: 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.  
DOCUMENT NUMBER: 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.  
TITLE: Antisense oligonucleotide inhibition of RANK expression.  
INVENTOR(S): Smith, Brian P.; Swartz, Lex M.  
PATENT APPLICATION: 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.  
SOURCE: 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.  
COPEN: UNKNAM  
DOCUMENT TYPE: 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6171860	P1	19991004	US 1999-435296	19991105
WO 2001034427	A1	20010417	WO 2000-0329828	20001030
R:	AK, AL, AM, AN, AO, AP, AQ, AR, AS, AT, AU, AV, AW, AX, AY, AZ, BA, BB, BC, BD, BE, BF, BG, BH, BI, BJ, BK, BL, BM, BN, BO, BP, BQ, BR, BS, BT, BU, BV, BW, BX, BY, BZ, CA, CB, CC, CD, CE, CF, CG, CH, CI, CJ, CK, CL, CM, CN, CO, CP, CQ, CR, CS, CT, CU, CV, CW, CX, CY, CZ, DA, DB, DC, DD, DE, DF, DG, DH, DI, DJ, DK, DL, DM, DN, DO, DP, DQ, DR, DS, DT, DU, DV, DW, DX, DY, DZ, EA, EB, EC, ED, EE, EF, EG, EH, EI, EJ, EK, EL, EM, EN, EO, EP, EQ, ER, ES, ET, EU, EV, EW, EX, EY, EZ, FA, FB, FC, FD, FE, FF, FG, FH, FI, FJ, FK, FL, FM, FN, FO, FP, FQ, FR, FS, FT, FU, FV, FW, FX, FY, FZ, GA, GB, GC, GD, GE, GF, GH, GI, GJ, GK, GL, GM, GN, GO, GP, GQ, GR, GS, GT, GU, GV, GW, GX, GY, GZ, HA, HB, HC, HD, HE, HF, HG, HH, HI, HJ, HK, HL, HM, HN, HO, HP, HQ, HR, HS, HT, HU, HV, HW, HX, HY, HZ, IA, IB, IC, ID, IE, IF, IG, IH, II, IJ, IK, IL, IM, IN, IO, IP, IQ, IR, IS, IT, IU, IV, IW, IX, IY, IZ, JA, JB, JC, JD, JE, JF, JG, JH, JI, JJ, JK, JL, JM, JN, JO, JP, JQ, JR, JS, JT, JU, JV, JW, JX, JY, JZ, KA, KB, KC, KD, KE, KF, KG, KH, KI, KJ, KK, KL, KM, KN, KO, KP, KQ, KR, KS, KT, KU, KV, KW, KX, KY, KZ, LA, LB, LC, LD, LE, LF, LG, LH, LI, LJ, LK, LL, LM, LN, LO, LP, LQ, LR, LS, LT, LU, LV, LW, LX, LY, LZ, MA, MB, MC, MD, ME, MF, MG, MH, MI, MJ, MK, ML, MM, MN, MO, MP, MQ, MR, MS, MT, MU, MV, MW, MX, MY, MZ, NA, NB, NC, ND, NE, NF, NG, NH, NI, NJ, NK, NL, NM, NO, NP, NQ, NR, NS, NT, NU, NV, NW, NX, NY, NZ, OA, OB, OC, OD, OE, OF, OG, OH, OI, OJ, OK, OL, OM, ON, OO, OP, OQ, OR, OS, OT, OU, OV, OW, OX, OY, OZ, PA, PB, PC, PD, PE, PF, PG, PH, PI, PJ, PK, PL, PM, PN, PO, PP, PQ, PR, PS, PT, PU, PV, PW, PX, PY, PZ, QA, QB, QC, QD, QE, QF, QG, QH, QI, QJ, QK, QL, QM, QN, QO, QP, QQ, QR, QS, QT, QU, QV, QW, QX, QY, QZ, RA, RB, RC, RD, RE, RF, RG, RH, RI, RJ, RK, RL, RM, RN, RO, RP, RQ, RR, RS, RT, RU, RV, RW, RX, RY, RZ, SA, SB, SC, SD, SE, SF, SG, SH, SI, SJ, SK, SL, SM, SN, SO, SP, SQ, SR, SS, ST, SU, SV, SW, SX, SY, SZ, TA, TB, TC, TD, TE, TF, TG, TH, TI, TJ, TK, TL, TM, TN, TO, TP, TQ, TR, TS, TU, TV, TW, TX, TY, TZ, UA, UB, UC, UD, UE, UF, UG, UH, UI, UJ, UK, UL, UM, UN, UO, UP, UQ, UR, US, UT, UU, UV, UW, UX, UY, UZ, VA, VB, VC, VD, VE, VF, VG, VH, VI, VJ, VK, VL, VM, VN, VO, VP, VQ, VR, VS, VT, VU, VV, VW, VX, VY, VZ, WA, WB, WC, WD, WE, WF, WG, WH, WI, WJ, WK, WL, WM, WN, WO, WP, WQ, WR, WS, WT, WU, WV, WW, WX, WY, WZ, XA, XB, XC, XD, XE, XF, XG, XH, XI, XJ, XK, XL, XM, XN, XO, XP, XQ, XR, XS, XT, XU, XV, XW, XX, XY, XZ, YA, YB, YC, YD, YE, YF, YG, YH, YI, YJ, YK, YL, YM, YN, YO, YP, YQ, YR, YS, YT, YU, YV, YW, YX, YY, YZ, ZA, ZB, ZC, ZD, ZE, ZF, ZG, ZH, ZI, ZJ, ZK, ZL, ZM, ZN, ZO, ZP, ZQ, ZR, ZS, ZT, ZU, ZV, ZW, ZX, ZY, ZZ			
EP 1228444	A1	20020404	EP 2000-974012	20001030
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, IT, LV, FI, RO, MK, CY, AL			

PRIORITY APPLN. INFO.: US 1999-435296 A 19991105  
WO 2000-0329828 W 20001030

AB Antisense oligonucleotides, compns., and methods are provided for inhibiting the expression of RANK (receptor activator of nuclear factor-kappa B), a receptor known to enhance T-cell growth and dendritic cell function. The compns. comprise antisense compds., particularly antisense oligonucleotides, targeted to nucleic acids encoding RANK. Primarily, oligonucleotides and oligonucleotides having 3'-methoxy groups which are 5'-phosphorylated inhibit the expression of RANK mRNA and protein. This is a significant improvement over previous antisense oligonucleotides which have been shown to inhibit RANK mRNA but not protein expression.

REFERENCE TO OTHER PUBLICATIONS: US 1999-435296 A 19991105  
WO 2000-0329828 W 20001030

L21 ANSWER IN: 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.  
ACCESSION NUMBER: 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.  
DOCUMENT NUMBER: 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.  
TITLE: Inhibiting the expression of RANK during differentiation and maturation of monocyte-derived dendritic cells using antisense oligonucleotide arrays and proteins.  
AUTHOR(S): de Nacur, Francis; Schenkels, Lynne; Grillo, Anthony; Miska, David; Jones, David; Smith, James; Hsu, John; Brown, John.  
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Michigan, Ann Arbor, MI, 48106-0602, USA.  
SOURCE: Journal of Biological Chemistry, 276(12), 3411-3416, 2001.  
FURTHER INFO: 1. The use of antisense oligonucleotides to inhibit the expression of NF- $\kappa$ B.

DOCUMENT TYPE: History  
LANGUAGE: English

AB **Dendritic cells** are specialized antigen-presenting cells that play a key role in the initiation of adaptive immune responses. The authors have used a combination of complementary DNA (cDNA) arrays and cDNA libraries to identify the genes expressed in human CD14<sup>+</sup> blood monocytes and dendritic cells. Analysis of gene expression changes at the RNA level using **oligonucleotide** microarrays complementary to 6,000 human genes revealed that approx. 4% of the genes were expressed in DCs. A total of 150 genes were regulated during DC differentiation or maturation. Most of these genes were not previously associated with DCs and include genes encoding secreted proteins as well as genes involved in cell adhesion, signaling, and lipid metab. Protein anal. of the same cell populations was done using two-dimensional gel electrophoresis. A total of 900 distinct protein spots were included, and 4% of them exhibited quant. changes during DC differentiation and maturation. Differentially expressed proteins were identified by mass spectrometry and found to represent proteins with Ca<sup>2+</sup> binding, fatty acid binding, or chaperone activities as well as proteins involved in cell motility. In addition, proteomic anal. provided an assessment of post-translational modifications. The chaperone protein, calnexin, was found to undergo cleavage, yielding a novel form. The combined **oligonucleotide** microarray and proteomic approaches have characterized genes associated with DC development and maturation and have allowed anal. of post-translational modifications of specific proteins as part of these processes.

REFERENCE COUNT: 10 (FULL-TEXT REFERENCES AVAILABLE FOR THIS REFERENCE AND CITATIONS AVAILABLE IN THE REF FORMAT)

I21 ANSWER 12-14-15-16-17-18-19-20-21-22-23-24-25-26-27-28-29-30-31-32-33-34-35-36-37-38-39-40-41-42-43-44-45-46-47-48-49-50-51-52-53-54-55-56-57-58-59-60-61-62-63-64-65-66-67-68-69-70-71-72-73-74-75-76-77-78-79-80-81-82-83-84-85-86-87-88-89-90-91-92-93-94-95-96-97-98-99-100-101-102-103-104-105-106-107-108-109-110-111-112-113-114-115-116-117-118-119-120-121-122-123-124-125-126-127-128-129-130-131-132-133-134-135-136-137-138-139-140-141-142-143-144-145-146-147-148-149-150-151-152-153-154-155-156-157-158-159-160-161-162-163-164-165-166-167-168-169-170-171-172-173-174-175-176-177-178-179-180-181-182-183-184-185-186-187-188-189-190-191-192-193-194-195-196-197-198-199-200-201-202-203-204-205-206-207-208-209-210-211-212-213-214-215-216-217-218-219-220-221-222-223-224-225-226-227-228-229-230-231-232-233-234-235-236-237-238-239-240-241-242-243-244-245-246-247-248-249-250-251-252-253-254-255-256-257-258-259-260-261-262-263-264-265-266-267-268-269-270-271-272-273-274-275-276-277-278-279-280-281-282-283-284-285-286-287-288-289-290-291-292-293-294-295-296-297-298-299-300-301-302-303-304-305-306-307-308-309-310-311-312-313-314-315-316-317-318-319-320-321-322-323-324-325-326-327-328-329-330-331-332-333-334-335-336-337-338-339-340-341-342-343-344-345-346-347-348-349-350-351-352-353-354-355-356-357-358-359-360-361-362-363-364-365-366-367-368-369-370-371-372-373-374-375-376-377-378-379-380-381-382-383-384-385-386-387-388-389-390-391-392-393-394-395-396-397-398-399-400-401-402-403-404-405-406-407-408-409-410-411-412-413-414-415-416-417-418-419-420-421-422-423-424-425-426-427-428-429-430-431-432-433-434-435-436-437-438-439-440-441-442-443-444-445-446-447-448-449-450-451-452-453-454-455-456-457-458-459-460-461-462-463-464-465-466-467-468-469-470-471-472-473-474-475-476-477-478-479-480-481-482-483-484-485-486-487-488-489-490-491-492-493-494-495-496-497-498-499-500-501-502-503-504-505-506-507-508-509-510-511-512-513-514-515-516-517-518-519-520-521-522-523-524-525-526-527-528-529-530-531-532-533-534-535-536-537-538-539-540-541-542-543-544-545-546-547-548-549-550-551-552-553-554-555-556-557-558-559-560-561-562-563-564-565-566-567-568-569-570-571-572-573-574-575-576-577-578-579-580-581-582-583-584-585-586-587-588-589-590-591-592-593-594-595-596-597-598-599-600-601-602-603-604-605-606-607-608-609-610-611-612-613-614-615-616-617-618-619-620-621-622-623-624-625-626-627-628-629-630-631-632-633-634-635-636-637-638-639-640-641-642-643-644-645-646-647-648-649-650-651-652-653-654-655-656-657-658-659-660-661-662-663-664-665-666-667-668-669-670-671-672-673-674-675-676-677-678-679-680-681-682-683-684-685-686-687-688-689-690-691-692-693-694-695-696-697-698-699-700-701-702-703-704-705-706-707-708-709-710-711-712-713-714-715-716-717-718-719-720-721-722-723-724-725-726-727-728-729-730-731-732-733-734-735-736-737-738-739-740-741-742-743-744-745-746-747-748-749-750-751-752-753-754-755-756-757-758-759-760-761-762-763-764-765-766-767-768-769-770-771-772-773-774-775-776-777-778-779-780-781-782-783-784-785-786-787-788-789-790-791-792-793-794-795-796-797-798-799-800-801-802-803-804-805-806-807-808-809-810-811-812-813-814-815-816-817-818-819-820-821-822-823-824-825-826-827-828-829-830-831-832-833-834-835-836-837-838-839-840-841-842-843-844-845-846-847-848-849-850-851-852-853-854-855-856-857-858-859-860-861-862-863-864-865-866-867-868-869-870-871-872-873-874-875-876-877-878-879-880-881-882-883-884-885-886-887-888-889-890-891-892-893-894-895-896-897-898-899-900-901-902-903-904-905-906-907-908-909-910-911-912-913-914-915-916-917-918-919-920-921-922-923-924-925-926-927-928-929-930-931-932-933-934-935-936-937-938-939-940-941-942-943-944-945-946-947-948-949-950-951-952-953-954-955-956-957-958-959-960-961-962-963-964-965-966-967-968-969-970-971-972-973-974-975-976-977-978-979-980-981-982-983-984-985-986-987-988-989-990-991-992-993-994-995-996-997-998-999-1000-1001-1002-1003-1004-1005-1006-1007-1008-1009-1010-1011-1012-1013-1014-1015-1016-1017-1018-1019-1020-1021-1022-1023-1024-1025-1026-1027-1028-1029-1030-1031-1032-1033-1034-1035-1036-1037-1038-1039-1040-1041-1042-1043-1044-1045-1046-1047-1048-1049-1050-1051-1052-1053-1054-1055-1056-1057-1058-1059-1060-1061-1062-1063-1064-1065-1066-1067-1068-1069-1070-1071-1072-1073-1074-1075-1076-1077-1078-1079-1080-1081-1082-1083-1084-1085-1086-1087-1088-1089-1090-1091-1092-1093-1094-1095-1096-1097-1098-1099-1100-1101-1102-1103-1104-1105-1106-1107-1108-1109-1110-1111-1112-1113-1114-1115-1116-1117-1118-1119-1120-1121-1122-1123-1124-1125-1126-1127-1128-1129-1130-1131-1132-1133-1134-1135-1136-1137-1138-1139-1140-1141-1142-1143-1144-1145-1146-1147-1148-1149-1150-1151-1152-1153-1154-1155-1156-1157-1158-1159-1160-1161-1162-1163-1164-1165-1166-1167-1168-1169-1170-1171-1172-1173-1174-1175-1176-1177-1178-1179-1180-1181-1182-1183-1184-1185-1186-1187-1188-1189-1190-1191-1192-1193-1194-1195-1196-1197-1198-1199-1200-1201-1202-1203-1204-1205-1206-1207-1208-1209-1210-1211-1212-1213-1214-1215-1216-1217-1218-1219-1220-1221-1222-1223-1224-1225-1226-1227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AP DNA from bacteria has a stimulatory effect on mammalian immune cells, which depend on the presence of unmethylated CpG dinucleotides in the bacterial DNA. In contrast, mammalian DNA has a low frequency of CpG dinucleotides, and these are mostly methylated; therefore, mammalian DNA does not have immuno-stimulatory activity. CpG DNA induces a strong T-helper-1-like inflammatory response. Accumulating evidence has revealed the therapeutic potential of CpG DNA as adjuvants for vaccination strategies for cancer, allergy and infectious diseases. Despite its prominent role, only the mol. mechanism by which CpG DNA activates immune cells remains unclear. Here, the authors demonstrate that the response to CpG DNA is mediated by a TLR-4-dependent, MyD88-dependent, IRAK-1-dependent pathway and not show any response to CpG DNA, indicating a lack of cross-reactivity of mammalian inflammatory cytokine production to CpG DNA stimulation of **dendritic cells**. TLR-4-deficient mice showed no difference in the overall effect of CpG DNA without any effect on serum pro-inflammatory cytokine levels. The in vitro CpG-DNA-induced T-helper type-1 response was also abolished in TLR-4-deficient mice. Thus, vertebrate immune systems appear to have evolved a specific TLR-4 receptor that distinguishes bacterial DNA from self-DNA.

L21 ANSWER 15 OF 15 ENBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

TITLE: Preexposure of murine macrophages to CpG-containing oligonucleotides results in nuclear factor- $\kappa$ B-dependent p50 homodimer-associated hypersecretory response.

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SUMMARY LANGUAGE: ENGLISH

**AB** Background. DNA containing the CpG motif is associated with immunomodulation of the innate immune response. Preexposure of macrophages to CpG DNA evokes a hyporesponsiveness to subsequent lipopolysaccharide (LPS) stimulation. We tested the hypothesis that this effect is due to decreased nuclear translocation of nuclear factor- $\kappa$ B (NF- $\kappa$ B). Methods. Murine macrophage-like RAW 264.7 cells were incubated with 100 .mu.g/mL CpG-containing oligonucleotides (CpG ODN) for 24 hours followed by restimulation with 1 .mu.g/mL LPS for 15 minutes. The cells were cotransfected with an NF- $\kappa$ B kappa.B sensitive luciferase reporter construct and a control vector plasmid. Cytoplasmic and nuclear extracts were analyzed for NF- $\kappa$ B. Results. CpG ODN treatment reduced LPS-induced NF- $\kappa$ B activity and nuclear translocation. Conclusions. NF- $\kappa$ B is involved in the regulation of macrophage function. CpG ODN treatment may alter macrophage function by decreasing NF- $\kappa$ B activity.



expression of the inhibitory  $\beta$  NF- $\kappa$ B  
homodimer and decreases NF- $\kappa$ B activity  
without inhibition of  $\kappa$ B kinase. NF- $\kappa$ B kinase protein kinase  
activity remains intact. These data suggest that the release  
dissociates the inhibitory  $\beta$  homodimer and the specific  
inhibitor.

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AB Dendritic cells (DC) constitute a complex system of uniquely well-equipped antigen-presenting cells that initiate and regulate immune responses. Extensive recent studies have improved our understanding of DC development, differentiation, activation, and function. DC exist as distinct subsets that differ in their lineage affiliation, surface molecule expression, and functional function. These factors seem to determine the T-cell priming stimulus and type 1 T cell response-T helper 1, T helper 2, and T regulatory-induced by DC (1). Evidence has accumulated that DC play an important role in both central and peripheral tolerance via various mechanisms, including induction of T-cell anergy, immune deviation, T regulatory cell activity, and promotion of activated T-cell apoptosis. Although many of the details of the molecular basis of DC **tolerogenicity** have yet to be elucidated, emerging information suggests that costimulatory molecule deficiency, expression of death-inducing ligands (in particular Fas (CD95) ligand), microenvironmental factors (in particular anti-inflammatory/immunosuppressive cytokines), and inhibition of gene transcription regulatory proteins (e.g., nuclear factor-kappaB) can impart **tolerogenic** potential to DC (2). Manipulation of DC by control of their maturation and differentiation, or genetic engineering of these cells to express immunosuppressive molecules, offers potential for therapy of allograft rejection and autoimmune disease. In this brief overview, we outline principles and methods for generation of "tolerogenic" DC and outcomes that have been reported in experimental models of transplantation rejection and autoimmunity.

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Fig. 1.  $\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$  currents in dendritic cells

genetically engineered using adenoviral (Ad) vectors to express immunosuppressive molecules that promote T cell unresponsiveness. The success of these T cell therapy of allograft rejection has been limited in part by the potential of the adenovirus to promote DC maturation and the inherent ability of the DC to undergo maturation following in vivo administration. DC maturation occurs via NF-kappaB-dependent mechanisms, which can be blocked by double-stranded "decoy" oligodeoxynucleotides (ODNs) containing binding sites for NF-kappaB. Herein, we describe the combined use of NF-kappaB ODNs and rAd vectors encoding CTLA4-Ig (Ad CTLA4-Ig) to generate stably immature murine myeloid DCs that secrete the potent costimulation blocking agent. These Ad CTLA4-Ig-transduced ODN DCs exhibit markedly reduced antigen presenting ability and promote apoptosis of activated T cells. In contrast, administration of Ad CTLA4-Ig B6-treated donor DCs to B6;H-2b recipients prior to transplant significantly prolongs MHC-mismatch heart grafts; B6.H-2b recipients heart allograft survival, with long-term (> 60 days) heart-specific graft survival in 40% of recipients. The mechanism responsible for DC **tolerogenicity**, which may involve a T cell-induced apoptosis of alloreactive T cells, do not lead to reduction of intra-graft Th cytokine responses. Use of NF-kappaB antisense decoys in combination with rAd encoding a potent costimulation blocking agent offers promise for therapy of allograft rejection or autoimmune disease with minimization of systemic immunosuppression.

L23 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:916972 CAPLUS

DOCUMENT NUMBER: 135:355016

TITLE: The use of **tolerogenic dendritic cells** for enhancing **tolerogenicity** in a host and methods for making the same

INVENTOR(S): Robbins, Paul E.; Li, Lina; Blann-Karls, Nick

PATENT ASSIGNEE(S): University of Pittsburgh of the Commonwealth System of Higher Education, USA

SOURCE: INT. J. Appl., 64 pp.  
1999:10001

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY APP. INT. NUMBER:

PATENT INFORMATION:

PATENT NO.	FIG.	DATE	APPLICATION NO.	DATE
WO 2001083713	A1	20011109	WO 2001-US13661	20010427
WO 2001083713	A1	20010914		
W:	AB, AC, AD, AE, AF, AG, AH, AI, AJ, AK, AL, AM, AN, AO, AP, AQ, AR, AS, AT, AU, AV, AW, AX, AY, AZ, BA, BB, BC, BD, BE, BF, BG, BH, BI, BJ, BK, BL, BM, BN, BO, BP, BQ, BR, BS, BT, BU, BV, BW, BX, BY, BZ, CA, CB, CC, CD, CE, CF, CG, CH, CI, CJ, CK, CL, CM, CN, CO, CP, CQ, CR, CS, CT, CU, CV, CW, CX, CY, CZ, DA, DB, DC, DD, DE, DF, DG, DH, DI, DJ, DK, DL, DM, DN, DO, DP, DQ, DR, DS, DT, DU, DV, DW, DX, DY, DZ, EA, EB, EC, ED, EE, EF, EG, EH, EI, EJ, EK, EL, EM, EN, EO, EP, EQ, ER, ES, ET, EU, EV, EW, EX, EY, EZ, FA, FB, FC, FD, FE, FF, FG, FH, FI, FJ, FK, FL, FM, FN, FO, FP, FQ, FR, FS, FT, FU, FV, FW, FX, FY, FZ, GA, GB, GC, GD, GE, GF, GG, GH, GI, GJ, GK, GL, GM, GN, GO, GP, GQ, GR, GS, GT, GU, GV, GW, GX, GY, GZ, HA, HB, HC, HD, HE, HF, HG, HH, HI, HJ, HK, HL, HM, HN, HO, HP, HQ, HR, HS, HT, HU, HV, HW, HX, HY, HZ, IA, IB, IC, ID, IE, IF, IG, IH, II, IJ, IK, IL, IM, IN, IO, IP, IQ, IR, IS, IT, IU, IV, IW, IX, IY, IZ, JA, JB, JC, JD, JE, JF, JG, JH, JI, JJ, JK, JL, JM, JN, JO, JP, JQ, JR, JS, JT, JU, JV, JW, JX, JY, JZ, KA, KB, KC, KD, KE, KF, KG, KH, KI, KJ, KK, KL, KM, KN, KO, KP, KQ, KR, KS, KT, KU, KV, KW, KX, KY, KZ, LA, LB, LC, LD, LE, LF, LG, LH, LI, LJ, LK, LL, LM, LN, LO, LP, LQ, LR, LS, LT, LU, LV, LW, LX, LY, LZ, MA, MB, MC, MD, ME, MF, MG, MH, MI, MJ, MK, ML, MM, MN, MO, MP, MQ, MR, MS, MT, MU, MV, MW, MX, MY, MZ, NA, NB, NC, ND, NE, NF, NG, NH, NI, NJ, NK, NL, NM, NN, NO, NP, NQ, NR, NS, NT, NU, NV, NW, NX, NY, NZ, OA, OB, OC, OD, OE, OF, OG, OH, OI, OJ, OK, OL, OM, ON, OO, OP, OQ, OR, OS, OT, OU, OV, OW, OX, OY, OZ, PA, PB, PC, PD, PE, PF, PG, PH, PI, PJ, PK, PL, PM, PN, PO, PP, PQ, PR, PS, PT, PU, PV, PW, PX, PY, PZ, QA, QB, QC, QD, QE, QF, QG, QH, QI, QJ, QK, QL, QM, QN, QO, QP, QQ, QR, QS, QT, QU, QV, QW, QX, QY, QZ, RA, RB, RC, RD, RE, RF, RG, RH, RI, RJ, RK, RL, RM, RN, RO, RP, RQ, RR, RS, RT, RU, RV, RW, RX, RY, RZ, SA, SB, SC, SD, SE, SF, SG, SH, SI, SJ, SK, SL, SM, SN, SO, SP, SQ, SR, SS, ST, SU, SV, SW, SX, SY, SZ, TA, TB, TC, TD, TE, TF, TG, TH, TI, TJ, TK, TL, TM, TN, TO, TP, TQ, TR, TS, TU, TV, TW, TX, TY, TZ, UA, UB, UC, UD, UE, UF, UG, UH, UI, UJ, UK, UL, UM, UN, UO, UP, UQ, UR, US, UT, UV, UW, UX, UY, UZ, VA, VB, VC, VD, VE, VF, VG, VH, VI, VJ, VK, VL, VM, VN, VO, VP, VQ, VR, VS, VT, VU, VV, VW, VX, VY, VZ, WA, WB, WC, WD, WE, WF, WG, WH, WI, WJ, WK, WL, WM, WN, WO, WP, WQ, WR, WS, WT, WU, WV, WW, WX, WY, WZ, XA, XB, XC, XD, XE, XF, XG, XH, XI, XJ, XK, XL, XM, XN, XO, XP, XQ, XR, XS, XT, XU, XV, XW, XX, XY, XZ, YA, YB, YC, YD, YE, YF, YG, YH, YI, YJ, YK, YL, YM, YN, YO, YP, YQ, YR, YS, YT, YU, YV, YW, YX, YY, YZ, ZA, ZB, ZC, ZD, ZE, ZF, ZG, ZH, ZI, ZJ, ZK, ZL, ZM, ZN, ZO, ZP, ZQ, ZR, ZS, ZT, ZU, ZV, ZW, ZX, ZY, ZZ			
RW:	GH, GM, KE, LS, MW, ME, SD, SI, SE, TG, TH, TN, AI, BA, BB, BC, BD, BE, BF, BG, BH, BI, BJ, BK, BL, BM, BN, BO, BP, BQ, BR, BS, BT, BU, BV, BW, BX, BY, BZ, CA, CB, CC, CD, CE, CF, CG, CH, CI, CJ, CK, CL, CM, CN, CO, CP, CQ, CR, CS, CT, CU, CV, CW, CX, CY, CZ, DA, DB, DC, DD, DE, DF, DG, DH, DI, DJ, DK, DL, DM, DN, DO, DP, DQ, DR, DS, DT, DU, DV, DW, DX, DY, DZ, EA, EB, EC, ED, EE, EF, EG, EH, EI, EJ, EK, EL, EM, EN, EO, EP, EQ, ER, ES, ET, EU, EV, EW, EX, EY, EZ, FA, FB, FC, FD, FE, FF, FG, FH, FI, FJ, FK, FL, FM, FN, FO, FP, FQ, FR, FS, FT, FU, FV, FW, FX, FY, FZ, GA, GB, GC, GD, GE, GF, GG, GH, GI, GJ, GK, GL, GM, GN, GO, GP, GQ, GR, GS, GT, GU, GV, GW, GX, GY, GZ, HA, HB, HC, HD, HE, HF, HG, HH, HI, HJ, HK, HL, HM, HN, HO, HP, HQ, HR, HS, HT, HU, HV, HW, HX, HY, HZ, IA, IB, IC, ID, IE, IF, IG, IH, II, IJ, IK, IL, IM, IN, IO, IP, IQ, IR, IS, IT, IU, IV, IW, IX, IY, IZ, JA, JB, JC, JD, JE, JF, JG, JH, JI, JJ, JK, JL, JM, JN, JO, JP, JQ, JR, JS, JT, JU, JV, JW, JX, JY, JZ, KA, KB, KC, KD, KE, KF, KG, KH, KI, KJ, KK, KL, KM, KN, KO, KP, KQ, KR, KS, KT, KU, KV, KW, KX, KY, KZ, LA, LB, LC, LD, LE, LF, LG, LH, LI, LJ, LK, LL, LM, LN, LO, LP, LQ, LR, LS, LT, LU, LV, LW, LX, LY, LZ, MA, MB, MC, MD, ME, MF, MG, MH, MI, MJ, MK, ML, MM, MN, MO, MP, MQ, MR, MS, MT, MU, MV, MW, MX, MY, MZ, NA, NB, NC, ND, NE, NF, NG, NH, NI, NJ, NK, NL, NM, NN, NO, NP, NQ, NR, NS, NT, NU, NV, NW, NX, NY, NZ, OA, OB, OC, OD, OE, OF, OG, OH, OI, OJ, OK, OL, OM, ON, OO, OP, OQ, OR, OS, OT, OU, OV, OW, OX, OY, OZ, PA, PB, PC, PD, PE, PF, PG, PH, PI, PJ, PK, PL, PM, PN, PO, PP, PQ, PR, PS, PT, PU, PV, PW, PX, PY, PZ, QA, QB, QC, QD, QE, QF, QG, QH, QI, QJ, QK, QL, QM, QN, QO, QP, QQ, QR, QS, QT, QU, QV, QW, QX, QY, QZ, RA, RB, RC, RD, RE, RF, RG, RH, RI, RJ, RK, RL, RM, RN, RO, RP, RQ, RR, RS, RT, RU, RV, RW, RX, RY, RZ, SA, SB, SC, SD, SE, SF, SG, SH, SI, SJ, SK, SL, SM, SN, SO, SP, SQ, SR, SS, ST, SU, SV, SW, SX, SY, SZ, TA, TB, TC, TD, TE, TF, TG, TH, TI, TJ, TK, TL, TM, TN, TO, TP, TQ, TR, TS, TU, TV, TW, TX, TY, TZ, UA, UB, UC, UD, UE, UF, UG, UH, UI, UJ, UK, UL, UM, UN, UO, UP, UQ, UR, US, UT, UV, UW, UX, UY, UZ, VA, VB, VC, VD, VE, VF, VG, VH, VI, VJ, VK, VL, VM, VN, VO, VP, VQ, VR, VS, VT, VU, VV, VW, VX, VY, VZ, WA, WB, WC, WD, WE, WF, WG, WH, WI, WJ, WK, WL, WM, WN, WO, WP, WQ, WR, WS, WT, WU, WV, WW, WX, WY, WZ, XA, XB, XC, XD, XE, XF, XG, XH, XI, XJ, XK, XL, XM, XN, XO, XP, XQ, XR, XS, XT, XU, XV, XW, XX, XY, XZ, YA, YB, YC, YD, YE, YF, YG, YH, YI, YJ, YK, YL, YM, YN, YO, YP, YQ, YR, YS, YT, YU, YV, YW, YX, YY, YZ, ZA, ZB, ZC, ZD, ZE, ZF, ZG, ZH, ZI, ZJ, ZK, ZL, ZM, ZN, ZO, ZP, ZQ, ZR, ZS, ZT, ZU, ZV, ZW, ZX, ZY, ZZ			

Priority claim to: US 2001/0111109, filed May 11, 2001, and US 2001/0111110, filed May 11, 2001.

AB The present invention provides a **tolerogenic dendritic cell** and a method for making the **tolerogenic** cell. In addition, the present invention provides a method for enhancing **tolerogenicity** in a host comprising administering **tolerogenic** dendritic cells to the present invention. The **tolerogenic** cell of the present invention comprises an exogenous nucleotide (N) which has one or more NF-kappaB binding sites. The **tolerogenic** cell of the present invention comprises a viral vector, and preferably an adenoviral vector, which does not affect the **tolerogenicity** of

L25 ALNOR 4 1  
ACCESSION NUMBER:  
DOCUMENT NUMBER:  
TITLE:  
**Mitotic mRNA microarray profiles of  
tolerogenic dendritic cells**  
AUTHOR(S):  
Sculci-Fore Corvesini, N.; Piazza, F.; Ho, E.;  
DiStefano, S.; LeMoult, C.; Dalla-Favera, R.;  
Corvesini, R.  
CORPORATE SOURCE:  
Department of Pathology, Columbia University, New  
York, NY, USA  
SOURCE:  
Human Immunology (2001), 62(10), 1068-1072  
CODEN: HUIMDQ; ISSN: 0198-8859  
PUBLISHER:  
Elsevier Science Inc.  
DOCUMENT TYPE:  
Journal  
LANGUAGE:  
English

REFERENCE COUNT: 41 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Dendritic cells (DCs) classically promote immune responses but can be manipulated to induce antigen-specific hypersensitization (1). The expression of costimulatory molecules (CD80, CD86, B7-1, B7-2) on DCs correlates with their capacity to induce or suppress immune responses. Expression of these molecules as well as NF- $\kappa$ B-dependent transcription of these genes is critical for DC **tolerogenicity** has been associated with impaired NF- $\kappa$ B-dependent transcription of costimulatory genes as well as NF- $\kappa$ B translocation to the nucleus. In this report, we demonstrate that double-stranded RNA (dsRNA) with the same sequence as the NF- $\kappa$ B NF- $\kappa$ B dsRNA (2) is sufficient to inhibit NF- $\kappa$ B translocation to the nucleus and NF- $\kappa$ B-dependent transcription of NF- $\kappa$ B target genes.

transcription of NF- $\kappa$ B target genes. Moreover, exposure of DC to the classical pathway of complement inhibited lipopolysaccharide (LPS)-induced nitric oxide production and maturation of DC. Treatment of bone marrow-derived DC progenitors with NF- $\kappa$ B DN selectively suppressed the cell-surface expression of costimulatory molecules without interfering with MHC class I or class II expression. Furthermore, NF- $\kappa$ B DN DC induced allogeneic donor-specific hyporesponsiveness in mixed leukocyte cultures, and this was associated with inhibition of TH1-type cytokine production. Finally, infusion of NF- $\kappa$ B DN-treated bone marrow-derived DC in allogeneic recipients prior to heart transplantation resulted in significant prolongation of allograft survival in the absence of immunosuppression. Specific interference with NF- $\kappa$ B and other transcriptional pathways involved in immune stimulation by DC using DN may provide a viable approach to promote tolerance induction in organ transplantation. (Am J Transplant 2002; 2: 1001-1010).

REFERENCE COUNT: 10. THERE ARE NO OTHER REFERENCES AVAILABLE FOR THIS ENTRY. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LIS NUMBER:	00000000000000000000
ACCESSION NUMBER:	00000000000000000000
DOCUMENT NUMBER:	00000000000000000000
TITLE:	Modulation of cellular dendritic cell survival by dendritic cells specifically engineered with NF-kappa B inhibitory expression plasmids and adenoviral vectors containing CTLA4-Ig.
AUTHOR:	Kumar P Andrew; Peng Liansha; Liang Xiaoyan; Chen Zongyou; Wang Huan; Ma Linlin; Hackstein Holger; Robbins Paul D; Thomsen Angus W; Fung John J; Qian Shiguang; Lu Lina
CORPORATE SOURCE:	Department of Surgery and Thomas E. Starzl Transplantation Institute, University of Pittsburgh Medical Center, University of Pittsburgh, Pittsburgh, PA 15213, USA.
CONTRACT NUMBER:	AI41011 (NIAID)
SOURCE:	JOURNAL OF IMMUNOLOGY, (2004 Sep 15) Vol 173, No 3, pp 3682-91. Journal code: 0022-1767. ISSN: 0221-1701.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; [JOURNAL ARTICLE]
LANGUAGE:	English
FILE SEGMENT:	Abstract Index Medicus Journals; Priority Journals
ENTRY MONTH:	.
ENTRY YEAR:	2004; Entry: 1; File: [unpublished] CTM 00000000000000000000 [unpublished] 00000000000000000000

AP-1 and NF- $\kappa$ B in dendritic cells (DCs) can be genetically engineered using adenoviral (Ad) vectors to express immunosuppressive molecules that promote T cell unresponsiveness. The success of these DCs for therapy of allograft rejection has been limited in part by the potential of the adenovirus to promote DC maturation and the inherent ability of the DC to undergo maturation following in vivo administration. DC maturation occurs via NF- $\kappa$ B-dependent mechanisms, which involve the assembly of double-stranded "decoy" oligodeoxynucleotides (ODNs) containing binding sites for NF- $\kappa$ B. Herein, we describe the combined use of NF- $\kappa$ B ODNs and rAd vectors encoding CTLA4-Ig (Ad CTLA4-Ig) to generate stably immature murine myeloid DCs that secrete the potent costimulation blocking agent. These Ad CTLA4-Ig-transduced ODN DCs exhibit markedly impaired allostimulatory ability and promote apoptosis of activated T cells. Furthermore, administration of Ad CTLA4-Ig ODN-treated donor DCs (C57BL/6; B10.H-2b) before transplant significantly prolongs MHC-mismatched (B10.H-2b; B10.H-2d) heart allograft survival, with long-term survival rates comparable to heart allograft survival in recipients of Ad CTLA4-Ig-transduced ODN DCs. These results suggest that **tolerogenicity**, which may be achieved by the use of Ad CTLA4-Ig-transduced T cells, and the use of Ad CTLA4-Ig-transduced ODN DCs may be used. Use of NF- $\kappa$ B antisense may provide an alternative to the use of a potent costimulation blocking agent in the therapy of allograft rejection or an immune response to transplantation; systemic immunosuppression.

155 ANCHOR: 100 MEDICINE DUPLICATE 2  
ACCESSION NUMBER: 100 MEDICINE  
DOCUMENT NUMBER: 100 MEDICINE PAPER-1 ID: 11-1001F  
TITLE: Manipulation of dendritic cells for  
tolerance induction in transplantation and auto-immune  
disease.  
AUTHOR: Lu, Liya; Thompson, Andrew W  
CORPORATE SOURCE: Thomas E. Starzl Transplantation Institute, Department of  
Surgery, University of Pittsburgh Medical Center,  
Pittsburgh, Pennsylvania 15261, USA. Email: liya.lu@upmc.edu  
CONTRACT NUMBER: ARL 11-0141  
DEPT: 100 MEDICINE  
DEPT: 100 MEDICINE  
SYNOPSIS: A review of the role of dendritic cells in transplantation tolerance and auto-immune disease.

PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; JOURNAL ARTICLE  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 2004  
 ENTRY DATE: Entered STM: 11/11/04  
 Last Updated STM: 11/11/04  
 Entered Medline: 11/11/04

**AB Dendritic cells** are constitutive complex system of uniquely well-suited antigen-presenting cells that initiate and regulate immune responses. Extensive research over the past decade has improved our understanding of DC development, differentiation, activation, and function. DC exist as distinct subsets that differ in their lineage affiliation, surface molecule expression, and functional potential. These factors seem to determine the T-cell signaling signals and type of T cell response-T helper 1, T helper 2, or T regulatory- induced by DC (1). Evidence has accumulated that DC play an important role in both central and peripheral tolerance via various mechanisms, including induction of T-cell anergy, immune deviation, T regulatory cell activity, and promotion of activated T-cell apoptosis. Although many of the details of the molecular basis of DC **tolerogenicity** have yet to be elucidated, emerging information suggests that costimulatory molecule deficiency, expression of death-inducing ligands (in particular Fas [CD95] ligand), microenvironmental factors (in particular anti-inflammatory/immunosuppressive cytokines), and inhibition of gene transcription regulatory proteins (e.g., nuclear factor-kappaB) can impact **tolerogenic** potential of DC (2). Manipulation of DC by control of their maturation and differentiation, or genetic engineering of these cells to express immunosuppressive molecules, offers potential for therapy of allograft rejection and other immune diseases. In this brief overview, we outline principles of dendritic cell generation as "tolerogenic" DC and summarize recent research progress in experimental models. Space constraints limit our discussion to certain topics.

125 ANWER 2004 MEDLINE DUPLICATE 3  
 ACCESSION NUMBER: 125 ANWER 2004 MEDLINE  
 DOCUMENT NUMBER: 125 ANWER 2004 MEDLINE ID: 10963964  
 TITLE: Induction of cardiac allograft survival using dendritic cells treated with NF-kB decoy oligonucleotides.  
 COMMENT: Erratum in: Mol Immunol. 2004 Sep;41(9):1297-1300.  
 Erratum in: Zhonghua Yi Xue Za Zhi. 2004;84(10):745-746.  
 AUTHOR: Giannoukakis N; Rankin C A; Qian S; Chen X; Peng L; Hamaoka J; Li W; Thomson A W; Fung J J; Reifkind J B; Leif L  
 CORPORATE SOURCE: Department of Molecular Genetics and Biochemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15261, USA.  
 CONTRACT NUMBER: 1R01HL001111  
 SOURCE: MEDLINE JOURNAL, May 11, 2004, Vol. 125, No. 10, pp. 1297-1300.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; JOURNAL ARTICLE  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 2004  
 ENTRY DATE: Entered STM: 11/11/04  
 Last Updated STM: 11/11/04  
 Entered Medline: 11/11/04

**AB Dendritic cells** are constitutive complex system of uniquely well-suited antigen-presenting cells that initiate and regulate immune responses. Extensive research over the past decade has improved our understanding of DC development, differentiation, activation, and function. DC exist as distinct subsets that differ in their lineage affiliation, surface molecule expression, and functional potential. These factors seem to determine the T-cell signaling signals and type of T cell response-T helper 1, T helper 2, or T regulatory- induced by DC (1). Evidence has accumulated that DC play an important role in both central and peripheral tolerance via various mechanisms, including induction of T-cell anergy, immune deviation, T regulatory cell activity, and promotion of activated T-cell apoptosis. Although many of the details of the molecular basis of DC **tolerogenicity** have yet to be elucidated, emerging information suggests that costimulatory molecule deficiency, expression of death-inducing ligands (in particular Fas [CD95] ligand), microenvironmental factors (in particular anti-inflammatory/immunosuppressive cytokines), and inhibition of gene transcription regulatory proteins (e.g., nuclear factor-kappaB) can impact **tolerogenic** potential of DC (2). Manipulation of DC by control of their maturation and differentiation, or genetic engineering of these cells to express immunosuppressive molecules, offers potential for therapy of allograft rejection and other immune diseases. In this brief overview, we outline principles of dendritic cell generation as "tolerogenic" DC and summarize recent research progress in experimental models. Space constraints limit our discussion to certain topics.





INVENTOR(S):	W. A. L. S. and others for making the same
PATENT ASSIGNEE(S):	Forlins, Paul L.; Lu, Lina; Giannoukakis, Nick
SOURCE:	University of Pittsburgh of the Commonwealth System of Higher Education, USA PCT Int. Appl., 64 pp. CODEN: F1XXD6
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY APP. NUM. COUNTRY:	1
PATENT INFORMATION:	

PATENT NO.	NAME	DATE	APPLICATING CO.	DATE
2,771,411	W. H. R. H. H. H.	1956-11-14	W. H. R. H. H. H.	1956-11-14
2,771,412	W. H. R. H. H. H.	1956-11-14	W. H. R. H. H. H.	1956-11-14

[illegible]

US 2002043564	AI	20020425	US 2001-644915	20010427
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PRIORITY APPLN. INFO.: US 2000-200479P P 20000428

AB The present invention relates to a **tolerogenic mammalian dendritic cells** (DCs) and methods for the prodn. of the **tolerogenic DCs**. In addn., the present invention provides a method for enhancing **tolerogenicity** in a host comprising administering the **tolerogenic mammalian DCs** of the present invention to the host. The **tolerogenic DCs** of the present invention comprise an **IL-10** expression cassette, **IL-10** which can be of more **NF- $\kappa$ B** than a wild type. The **tolerogenic DCs** of the present invention may further comprise a **viral vector**, **IL-10** is only in a **viral vector**, which does not affect the **tolerogenicity** of the **tolerogenic DCs** when present therein. Enhancing **tolerogenicity** in a host is useful for prolonging **allograft survival** and/or treating **inflammatory related diseases**, **autoimmune related diseases**.

[illegible]

ACCESS TO MEDICAL RECORDS: 1: 11/1/82 2: 11/1/82

DOCUMENT NUMBER: 100-3-346-

TITLE: Characterization of regulatory properties of  
tolerogenic dendritic cells

AUTHOR(S): Suzin-Poon, Cortesini, R.; Flanagan, E.; Ho, E.; Gubotariu, R.; LeMabault, J.; Palla-Bauer, E.; Cortesini, R.

CORPORATE SOURCE: Department of Pathology, Florida University, New York, NY, USA

PUBLISHED BY: 

Figure 1. Schematic representation of the experimental design. The subjects were divided into two groups: the control group and the experimental group. The control group was divided into two subgroups: the control group and the control group. The experimental group was divided into two subgroups: the experimental group and the experimental group. The control group was divided into two subgroups: the control group and the control group. The experimental group was divided into two subgroups: the experimental group and the experimental group.

**TABLE 1**

AP Dendritic cells are known to be highly antigenic, well as antigen presenting cells. In this study we have illustrated that APCs from the spleen of anti-CD3-treated mice suppress T cells become tolerogenic, and suppress energy. In characterizing the mol. changes associated with tolerogenic APC, the mRNA profile of K5-1 dendritic cells was analyzed along with T helper and T suppressor cell gene analysis. This study now provides evidence that immature dendritic cells suppressively T suppressor



L15 ANSWER 1 OF 2 PATENT COPYRIGHT LAW

ACCESSION NUMBER: 101-101-101

DOCUMENT NUMBER: 101-101-101

TITLE: Dendritic cells (DC) classically promote immune responses but can be manipulated to induce antigen-specific hyporesponsiveness in vitro. The expression of costimulatory moles (CD40, CD86, CD80) at the DC cell surface correlates with their capacity to induce or suppress immune responses. Expression of these moles is assoc. with NF-kappa-B-dependent transcription of their genes. DC **tolerogenicity** has been assoc. with impaired NF-kappa-B-dependent transcription of costimulatory genes as well as NF-kappa-B translocation to the nucleus. In this report, we demonstrate that a non-transcribed oligonucleotide decoy can block sites for NF-kappa-B (NF-kappa-B ODN) are efficiently incorporated by bone marrow-derived DC and specifically inhibit NF-kappa-B-dependent transcription of a reporter gene. Moreover, exposure of DC to the oligonucleotide decoys inhibited lipopolysaccharide (LPS)-induced nitric oxide prodn., a marker of DC maturation. Treatment of bone marrow-derived DC progenitors with NF-kappa-B ODN selectively suppressed the cell-surface expression of costimulatory moles without interfering with MHC class I or class II expression. Furthermore, NF-kappa-B ODN DC induced allogeneic donor-specific hyporesponsiveness in mixed leukocyte cultures, and this was assoc. with inhibition of Th1-type cytokine prodn. Finally, infusion of NF-kappa-B ODN-modified bone marrow-derived DC into allogeneic recipients prior to heart transplantation resulted in significant prolongation of allograft survival in the absence of immunosuppression. Specific interference with NF-kappa-B and other transcriptional pathways involved in immune stimulation in DC using ODN decoy approaches could be one means to promote tolerance induction in organ transplantation. (J Biol Chem 275:101-101)

AUTHOR(S): Giannoukakis, Nick; Graham, C. Andrew; Qian, Shiguang; Jiao, Zhongyuan; Peng, Liansha; Harnaha, Jo; Li, Wei; Thomson, Angus W.; Fung, John J.; Robbins, Paul D.; Lu, Lina

CORPORATE SOURCE: Department of Molecular Genetics and Biochemistry, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: Molecular Therapy (2000), 1(5, Pt. 1), 430-437  
CODEN: MTHOKK; ISSN: 1525-0016

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Dendritic cells (DC) classically promote immune responses but can be manipulated to induce antigen-specific hyporesponsiveness in vitro. The expression of costimulatory moles (CD40, CD86, CD80) at the DC cell surface correlates with their capacity to induce or suppress immune responses. Expression of these moles is assoc. with NF-kappa-B-dependent transcription of their genes. DC **tolerogenicity** has been assoc. with impaired NF-kappa-B-dependent transcription of costimulatory genes as well as NF-kappa-B translocation to the nucleus. In this report, we demonstrate that a non-transcribed oligonucleotide decoy can block sites for NF-kappa-B (NF-kappa-B ODN) are efficiently incorporated by bone marrow-derived DC and specifically inhibit NF-kappa-B-dependent transcription of a reporter gene. Moreover, exposure of DC to the oligonucleotide decoys inhibited lipopolysaccharide (LPS)-induced nitric oxide prodn., a marker of DC maturation. Treatment of bone marrow-derived DC progenitors with NF-kappa-B ODN selectively suppressed the cell-surface expression of costimulatory moles without interfering with MHC class I or class II expression. Furthermore, NF-kappa-B ODN DC induced allogeneic donor-specific hyporesponsiveness in mixed leukocyte cultures, and this was assoc. with inhibition of Th1-type cytokine prodn. Finally, infusion of NF-kappa-B ODN-modified bone marrow-derived DC into allogeneic recipients prior to heart transplantation resulted in significant prolongation of allograft survival in the absence of immunosuppression. Specific interference with NF-kappa-B and other transcriptional pathways involved in immune stimulation in DC using ODN decoy approaches could be one means to promote tolerance induction in organ transplantation. (J Biol Chem 275:101-101)

REFERENCE: 1. (J Biol Chem 275:101-101) REFERENCE AVAILABLE FOR THIS DOCUMENT AND FULL-TEXT AVAILABLE IN THE PDF FORMAT

L15 ANSWER 1 OF 2 PATENT COPYRIGHT LAW

ACCESSION NUMBER: 101-101-101

DOCUMENT NUMBER: 101-101-101

TITLE: The use of **tolerogenic** dendritic cells for enhancing **tolerogenicity** in a host and methods for making the same

INVENTOR(S): Fung, John J.; Lu, Lina; Giannoukakis, Nick  
PATENT ASSIGNER(S): University of Pittsburgh of the Commonwealth System of Higher Education, USA

SOURCE: Int. Appl., 00/000000  
CLASS: F100

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY APP. NUM. COUNT: 1

PATENT INFORMATION:

WO 2001/03661  
WO 2001/03661

AL 2001/03661  
AL 2001/03661

WO 2001-US13661 20010427

W: AE, AG, AI, AM, AT, AU, AZ, BA, BB, BC, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DO, EE, ES, FI, GB, GD, GE, GH, GM,  
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,  
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NE, NL, NO, NZ,  
RU, SD, SE, SG, SI, SK, SL, SN, SV, TH, TT, TZ, UA, UG, UZ, VN,  
YU, ZA, ZW, AM, AZ, BA, BB, BC, BD, BE, BF, BG, BH, BI, BJ, BR,  
BW, BY, BZ, CA, CB, CC, CD, CE, CF, CG, CH, CI, CL, CM, CN, CO, CR,  
RW: GH, GM, KE, LS, MW, MZ, SD, SI, SO, SZ, TG, TH, TN, TR, TT, TZ, UA, UG, UZ, VN,  
DE, DK, ES, FI, FR, GB, GR, HU, IL, IN, IT, JP, KE, KG, KR, KZ, RU,  
BJ, CF, CH, CI, CN, CO, CR, CU, EE, EG, ES, FI, FR, GB, GR, GU, HT, IL, IN, IT, JP, KE, KG, KR, KZ, RU,  
US 2001/03661 AL 2001/03661 WO 2001-US13661 20010427

PRIORITY AFFILIATION:

AB The present invention relates to a **tolerogenic** mammalian dendritic cell (DC) comprising the protein of the **tolerogenic** DC. In addition, the present invention provides a method for enhancing **tolerogenicity** in a host comprising administering the **tolerogenic** mammalian DCs of the present invention to the host. The **tolerogenic** DCs of the present invention comprise an oligodeoxynucleotide (ODN) which has one or more NF- $\kappa$ B binding sites. The **tolerogenic** DCs of the present invention may further comprise a viral vector, and preferably an adenoviral vector, which does not affect the **tolerogenicity** of the **tolerogenic** DCs when present therein. Enhanced **tolerogenicity** in a host is useful for prolonging foreign graft survival and for treating inflammatory related diseases, such as autoimmune diseases.

114 ANNEXE I : 1-10  
 ACCESS: 1. DOCUMENT:  
 TITLE: 1-10  
 INVENTOR: 1-10  
 PATENT ASSISTANCE: 1-10  
 SOURCE: 1-10  
 DOCUMENT TYPE: 1-10  
 LANGUAGE: 1-10  
 FAMILY ACC. NUM. COUNT: 1-10  
 PATENT INFORMATION: 1-10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6469144	B1	20021022	US 1997-824683	19970631
CA 2249206	A2	19971003	US 1997 1249206	19970631
US 2002123116	A1	20020611	US 1997-254913	19970631
US 6469144	A1	20020611	US 1997-254914	19970631
PRIORITY APPL. REF. 1:			US 1997-254913	A1 19970631
			US 1997-254914	B1 19970631
			US 1997-254915	A1 19970631
			US 1997-254916	A1 19970631
			US 1997-254917	A1 19970631
			US 1997-254918	A1 19970631
			US 1997-254919	A1 19970631
			US 1997-254920	A1 19970631
			US 1997-254921	A1 19970631
			US 1997-254922	A1 19970631
			US 1997-254923	A1 19970631
			US 1997-254924	A1 19970631
			US 1997-254925	A1 19970631
			US 1997-254926	A1 19970631
			US 1997-254927	A1 19970631
			US 1997-254928	A1 19970631
			US 1997-254929	A1 19970631
			US 1997-254930	A1 19970631
			US 1997-254931	A1 19970631
			US 1997-254932	A1 19970631
			US 1997-254933	A1 19970631
			US 1997-254934	A1 19970631
			US 1997-254935	A1 19970631
			US 1997-254936	A1 19970631
			US 1997-254937	A1 19970631
			US 1997-254938	A1 19970631
			US 1997-254939	A1 19970631
			US 1997-254940	A1 19970631
			US 1997-254941	A1 19970631
			US 1997-254942	A1 19970631
			US 1997-254943	A1 19970631
			US 1997-254944	A1 19970631
			US 1997-254945	A1 19970631
			US 1997-254946	A1 19970631
			US 1997-254947	A1 19970631
			US 1997-254948	A1 19970631
			US 1997-254949	A1 19970631
			US 1997-254950	A1 19970631
			US 1997-254951	A1 19970631
			US 1997-254952	A1 19970631
			US 1997-254953	A1 19970631
			US 1997-254954	A1 19970631
			US 1997-254955	A1 19970631
			US 1997-254956	A1 19970631
			US 1997-254957	A1 19970631
			US 1997-254958	A1 19970631
			US 1997-254959	A1 19970631
			US 1997-254960	A1 19970631
			US 1997-254961	A1 19970631
			US 1997-254962	A1 19970631
			US 1997-254963	A1 19970631
			US 1997-254964	A1 19970631
			US 1997-254965	A1 19970631
			US 1997-254966	A1 19970631
			US 1997-254967	A1 19970631
			US 1997-254968	A1 19970631
			US 1997-254969	A1 19970631
			US 1997-254970	A1 19970631
			US 1997-254971	A1 19970631
			US 1997-254972	A1 19970631
			US 1997-254973	A1 19970631
			US 1997-254974	A1 19970631
			US 1997-254975	A1 19970631
			US 1997-254976	A1 19970631
			US 1997-254977	A1 19970631

AB The author discloses the cloning and sequence characterization for the tumor necrosis factor family member Apo-3 and Apo-2 ligand inhibitor (Apo-2L), an extra-cellular fragment of Apo-3 generated by alternative splicing. In addition, the author discloses the apoptotic function of Apo-3, a partial characterization of its signaling pathway, and tissue specificity for its expression.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	2002:770147	CAPLUS
DOCUMENT NUMBER:	137:068987	
TITLE:	Apo-B protein, a new member of TTRP family involved in apoptosis and related signaling and differentiation	
INVENTOR(S):	Arredondo, Avelino	
PATENT APLICHER(S):	Arredondo, Avelino	
SOURCE:	1997, 34: 1000-1004	
	TIPO: JOURNAL	
DOCUMENT TYPE:	Article	
LANGUAGE:	English	
FAMILY AND INTL. APP.:	1	
PATENT APPLICATION:	1	

PATENT NO.	FILED	DATE	APPLICATION NO.	DATE
US 6461786	RI	11/11/00	US 1999-42168	19990311
US 2002160117	AI	10/21/01	US 1999-42168	20020221
PRIORITY APPLN. INFO.:			US 1996-14649P	19960401
			US 1996-14649P	19960401
			US 1996-14649P	19960401

AB Novel polypeptides, designated Ag-1, which are capable of stimulating or inducing apoptosis are provided. Ag-1 is a new member of the TNF family exhibiting sequence homology with TNF $\alpha$ , TNF $\beta$ , and TNF $\gamma$ , and contains extracellular cysteine-rich repeats and cytoplasmic domains. The cDNA for Ag-1 is 1.5 kb long and encodes Ag-1 protein consisting of 213 amino acids. Ag-1 is secreted as a homotrimeric protein. Recombinant Ag-1 protein, purified from *Escherichia coli*, induces apoptosis in human promyelocytic leukemia cells, HL-60 cells, and human colon carcinoma cells, CEM-CM cells, and human epidermal carcinoma cells, A431 cells, and human melanoma cells, M1 cells. The recombinant Ag-1 protein also induces apoptosis in human myeloid leukemia cells, U937 cells, and human myeloid leukemia cells, THP-1 cells.

CPF32/yama. App-8 can activate NF-kappa-B activation.  
 REFERENCE COUNT: 274 THERE ARE 274 CITED REFERENCES AVAILABLE FOR  
 THIS REPORT. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L14 ANSWER 3 OF 16 CAPINT COPYRIGHT 1998 ACM  
 ACCESSION NUMBER: 19980046 CAPINT  
 DOCUMENT NUMBER: 19980046  
 TITLE: Inhibition of NF-kappa-B by triterpene compositions  
 INVENTOR(S): Patterson, Brian W.; Hildes, Mary E.; Patterson, Brian W.; Hildes, Mary E.; Hildes, Mary E.; Hildes, Mary E.  
 PATENT ASSIGNEE(S): Research Development Foundation, USA  
 SOURCE: PCT Int. Appl., 1998 01.  
 CODEN: F1XXDE  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6444233	B1	20020903	US 1999-314691	19990519
PRIORITY APPLN. INFO.:			US 1998-85997P	P 19980519
			US 1998-99066P	F 19980903

OTHER SOURCE(S): MARPAT 137:110215  
 AB The invention provides novel saponin mixts. and compds. which are isolated from the species *Asasia victorialis* and methods for their use. These compds. may contain a triterpene moiety, such as a saponin, or a saponin, to which a triterpene moiety is attached. The mixts. and compds. are useful for the treatment of apoptosis and other diseases. The invention also provides a method for the treatment of a disease by administering a saponin or a saponin derivative to a patient.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR  
 THIS REPORT. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L14 ANSWER 4 OF 16 CAPINT COPYRIGHT 1998 ACM  
 ACCESSION NUMBER: 19980046 CAPINT  
 DOCUMENT NUMBER: 19980046  
 TITLE: Inhibition of NF-kappa-B by triterpene compositions  
 INVENTOR(S): Patterson, Brian W.; Hildes, Mary E.  
 PATENT ASSIGNEE(S): Research Development Foundation, USA  
 SOURCE: PCT Int. Appl., 1998 01.  
 CODEN: F1XXDE  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
W: AB, AC, AD, AE, AF, AG, AH, AI, AJ, AK, AL, AM, AN, AO, AP, AQ, AR, AS, AT, AU, AV, AW, AX, AY, AZ, BA, BB, BC, BD, BE, BF, BG, BH, BI, BJ, BK, BL, BM, BN, BO, BP, BQ, BR, BS, BT, BU, BV, BW, BX, BY, BZ, CA, CB, CC, CD, CE, CF, CG, CH, CI, CJ, CK, CL, CM, CN, CO, CP, CQ, CR, CS, CT, CU, CV, CW, CX, CY, CZ, DA, DB, DC, DD, DE, DF, DG, DH, DI, DJ, DK, DL, DM, DN, DO, DP, DQ, DR, DS, DT, DU, DV, DW, DX, DY, DZ, EA, EB, EC, ED, EE, EF, EG, EH, EI, EJ, EK, EL, EM, EN, EO, EP, EQ, ER, ES, ET, EU, EV, EW, EX, EY, EZ, FA, FB, FC, FD, FE, FF, FG, FH, FI, FJ, FK, FL, FM, FN, FO, FP, FQ, FR, FS, FT, FU, FV, FW, FX, FY, FZ, GA, GB, GC, GD, GE, GF, GH, GI, GJ, GK, GL, GM, GN, GO, GP, GQ, GR, GS, GT, GU, GV, GW, GX, GY, GZ, HA, HB, HC, HD, HE, HF, HG, HH, HI, HJ, HK, HL, HM, HN, HO, HP, HQ, HR, HS, HT, HU, HV, HW, HX, HY, HZ, IA, IB, IC, ID, IE, IF, IG, IH, II, IJ, IK, IL, IM, IN, IO, IP, IQ, IR, IS, IT, IU, IV, IW, IX, IY, IZ, JA, JB, JC, JD, JE, JF, JG, JH, JI, JJ, JK, JL, JM, JN, JO, JP, JQ, JR, JS, JT, JU, JV, JW, JX, JY, JZ, KA, KB, KC, KD, KE, KF, KG, KH, KI, KJ, KK, KL, KM, KN, KO, KP, KQ, KR, KS, KT, KU, KV, KW, KX, KY, KZ, LA, LB, LC, LD, LE, LF, LG, LH, LI, LJ, LK, LL, LM, LN, LO, LP, LQ, LR, LS, LT, LU, LV, LW, LX, LY, LZ, MA, MB, MC, MD, ME, MF, MG, MH, MI, MJ, MK, ML, MN, MO, MP, MQ, MR, MS, MT, MU, MV, MW, MX, MY, MZ, NA, NB, NC, ND, NE, NF, NG, NH, NI, NJ, NK, NL, NM, NO, NP, NQ, NR, NS, NT, NU, NV, NW, NX, NY, NZ, OA, OB, OC, OD, OE, OF, OG, OH, OI, OJ, OK, OL, OM, ON, OO, OP, OQ, OR, OS, OT, OU, OV, OW, OX, OY, OZ, PA, PB, PC, PD, PE, PF, PG, PH, PI, PJ, PK, PL, PM, PN, PO, PP, PQ, PR, PS, PT, PU, PV, PW, PX, PY, PZ, QA, QB, QC, QD, QE, QF, QG, QH, QI, QJ, QK, QL, QM, QN, QO, QP, QQ, QR, QS, QT, QU, QV, QW, QX, QY, QZ, RA, RB, RC, RD, RE, RF, RG, RH, RI, RJ, RK, RL, RM, RN, RO, RP, RQ, RR, RS, RT, RU, RV, RW, RX, RY, RZ, SA, SB, SC, SD, SE, SF, SG, SH, SI, SJ, SK, SL, SM, SN, SO, SP, SQ, SR, SS, ST, SU, SV, SW, SX, SY, SZ, TA, TB, TC, TD, TE, TF, TG, TH, TI, TJ, TK, TL, TM, TN, TO, TP, TQ, TR, TS, TU, TV, TW, TX, TY, TZ, UA, UB, UC, UD, UE, UF, UG, UH, UI, UJ, UK, UL, UM, UN, UO, UP, UQ, UR, US, UT, UV, UW, UX, UY, UZ, VA, VB, VC, VD, VE, VF, VG, VH, VI, VJ, VK, VL, VM, VN, VO, VP, VQ, VR, VS, VT, VU, VW, VX, VY, VZ, WA, WB, WC, WD, WE, WF, WG, WH, WI, WJ, WK, WL, WM, WN, WO, WP, WQ, WR, WS, WT, WU, WV, WW, WX, WY, WZ, XA, XB, XC, XD, XE, XF, XG, XH, XI, XJ, XK, XL, XM, XN, XO, XP, XQ, XR, XS, XT, XU, XV, XW, XX, XY, XZ, YA, YB, YC, YD, YE, YF, YG, YH, YI, YJ, YK, YL, YM, YN, YO, YP, YQ, YR, YS, YT, YU, YV, YW, YX, YY, YZ, ZA, ZB, ZC, ZD, ZE, ZF, ZG, ZH, ZI, ZJ, ZK, ZL, ZM, ZN, ZO, ZP, ZQ, ZR, ZS, ZT, ZU, ZV, ZW, ZX, ZY, ZZ				

PRIORITY APPLN. INFO.:

CHEER, J. 1993. *Journal of Great Lakes Research* 19:1-2.

AB The invention provides for a carrier molecule that is characterized by a variety of chemical, physical, and biological properties that inhibit NF- $\kappa$ B. These properties may include a carrier moiety that renders the monoterpenoid compound permeable. The carrier may include a sugar, a polymer, a lipid, a steroid, and/or monoterpenoid moieties. The compound may also contain additional chemical functionalities. Methods for using these compounds to prevent and treat a wide range of inflammatory conditions, e.g., proinflammatory inflammatory conditions are described.

L14 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:391856 CAF100

DOCUMENT NUMBER: 136:396944

TITLE: Preparation of T cell line expressing HIV-1gag and RT<sup>+</sup> and the use of the cell line as a template

INVENTOR(S): MANNING, BRUCE; MANNING, WILLIAM; MANNING, ROBERT

PATENT ASSIGNMENT TO: The United States, et al., et al.

SOURCE: THE NEW YORK TIMES, 1964, 11/11, 1, 11.

DOCUMENT TYPE: ☐ OTHER ☒ JOURNAL

LANGUAGE: English

FAMILY NAME: \_\_\_\_\_

PATENT INFORMATION:

PATENT NO.	FILE	DATE	APPLICATION NO.	DATE
WO 2004/04104-	A1	1. 12.2003	NO 2001-JP10018	2001.11.16

W: AE, AG, AL, AN, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CE, DE, DK, DZ, EC, EE, ES, FI, GE, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,  
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL,  
PT, RO, RU, SD, SE, SG, SI, SK, SL, TH, TR, TT, TZ, UA, UG,  
US, UZ, VN, YU, ZA, ZM, ZW, AZ, BY, KG, KZ, MD, RU, TJ, TM

FW: GE, GM, KE, LS, MW, NZ, SD, SL, SZ, TE, TG, TN, TR, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, MC, NL, PT, SE, TF,  
BF, BJ, CF, CG, CI, CM, GA, GN, HQ, HR, IL, IN, JP, JO, KL, KU

AU 2002014307      A5      2002.7827      A5 2002-14307      2002.7827

PRIORITY APPLN. INFO.:            Y A - M - S       R - M - S

REFERENCE FORM:                 INDEX APP. WITH REFERENCES AVAILABLE FOR THIS  
REFORM. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER C ✓ E ✓ D ✓ B ✓ A ✓

MOORE, J. R. 1990. *Journal of Great Lakes Research* 16:111-114.

DOCUMENT NUMBER : 100-10449

TITLE: Inhibition of cellular allograft survival using  
recombinant adenovirus with NF-kappa-B gene  
oligonucleotide therapy

AUTHOR(S): Elan, David; Elor, Eyal; Elor, Yoram; Elor, Yoram;  
Elor, Yoram; Elor, Yoram; Elor, Yoram; Elor, Yoram;  
Elor, Yoram; Elor, Yoram; Elor, Yoram; Elor, Yoram;  
Elor, Yoram; Elor, Yoram; Elor, Yoram; Elor, Yoram;  
Elor, Yoram; Elor, Yoram; Elor, Yoram; Elor, Yoram;

[illegible]

Table 1. *Salmonella* serotypes and their associated diseases

Figure 1. The effect of the concentration of the *Agrobacterium* suspension on the transformation efficiency of *Agrobacterium* strains. The *Agrobacterium* strains were grown in the YEA medium for 24 h at 28 °C. The cell concentration of the strains was adjusted to 1.0 × 10<sup>8</sup> cells/ml. The cell suspension was mixed with the plant tissue and the transformation efficiency was determined. The results were expressed as the mean ± SD of three independent experiments. The asterisks indicate the significant difference between the strains at the same concentration of the cell suspension.











ACCESSION NUMBER: 1994:01394- TAIHAN  
 DOCUMENT NUMBER: 111:2348  
 TITLE: In vitro study of functional involvement of Sp1, NF-kappa.B/kel, and AP1 in p18 12-myristate 13-acetate-mediated HIV-1 long terminal repeat activation.  
 AUTHOR(S): Li, Yuhli; Nak, Hida; Branna, Robert B., Jr.  
 CORPORATE SOURCE: Cold Spring Harbor Lab., Cold Spring Harbor, New York, NY, 11724, USA  
 J EFIN: 111:2348  
 PUBLISHER: Cold Spring Harbor Laboratory and Cold Spring Harbor Laboratory Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB We examd. the cooperative activity between the Sp1 and NF-kappa.B/Rel sites of the human immunodeficiency virus type 1 long terminal repeat in response to phorbol 12-myristate 13-acetate (PMA) stimulation in an in vitro transcription assay. Sp1 sites alone do not account for the activation induced by PMA. When mutations in Sp1 sites were combined with mutations in the NF-kappa.B/Rel sites, a dramatic redn. in PMA-induced transcriptional activity was obsd. This redn. was much greater than the redn. assocd. with mutations involving only the NF-kappa.B/Rel sites. This finding suggests that there is functional cooperation between Sp1 and NF-kappa.B/Rel and that this is one possible mechanism for transcription activation by NF-kappa.B/Rel. The three AP1 sites in the long terminal repeat region of the long terminal repeat, however, seem to be uninvolved in the earliest events of transcriptional activation by PMA.

L14 ANSWER 14 1994:01394- TAIHAN  
 ACCESSION NUMBER: 1994:01394- TAIHAN  
 DOCUMENT NUMBER: 111:2348  
 TITLE: Transcription factor A120 regulates human immunodeficiency virus type 1 gene expression.  
 AUTHOR(S): Bergant, David T.; Aronoff, Adam, B.; Duckett, Colin A.; Nakel, Gary L.  
 CORPORATE SOURCE: Howard Hughes Medical Institute, University Michigan, Ann Arbor, MI, 48109-3636, USA  
 SOURCE: Journal of Virology 1994, 68(10), 6820-3  
 JOLIN: JOVIAN; ISSN: 0022-538X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Human immunodeficiency virus type 1 (HIV-1) gene expression is regulated by an enhancer region composed of multiple potential cis-acting regulatory sites. Here, we describe binding sites for the transcription factor A120 in the HIV-1 long terminal repeat which modulate HIV enhancer function. One site is embedded within the two previously identified kappa.B elements, and a second site is detected further downstream. Glucocorticoid repression and electrophoretic mobility shift assay experiments indicated that A120 binds to the site between the kappa.B elements. Interestingly, A120 and NF-kappa.B interact in a complex in a mutually exclusive manner. Mutational analysis of the HIV enhancer region showed that A120 binds to the enhancer region in a manner that is distinct from the kappa.B elements.

L14 ANSWER 14 1994:01394- TAIHAN  
 ACCESSION NUMBER: 1994:01394- TAIHAN  
 DOCUMENT NUMBER: 111:2348  
 TITLE: Regulation of HIV-1 gene expression by the HIV-1 enhancer region.  
 AUTHOR(S): Bergant, David T.; Aronoff, Adam, B.; Duckett, Colin A.; Nakel, Gary L.



# PALM INTRANET

Day : Thursday  
Date: 11/21/2002  
Time: 10:36:16

## Inventor Name Search

Enter the **first few letters** of the Inventor's Last Name.  
Additionally, enter the **first few letters** of the Inventor's First name.

**Last Name****First Name**

Robbins

Paul

Search

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PALM INTRANET

Day : Thursday  
Date: 11/21/2002  
Time: 10:39:03

## Inventor Name Search

Enter the **first few letters** of the Inventor's Last Name.  
Additionally, enter the **first few letters** of the Inventor's First name.

**Last Name****First Name**

Lu

Lina

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LE ANSWER 1 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INTERNATIONAL  
 ACCESSION NUMBER: 2002:345247 BIOSIS  
 DOCUMENT NUMBER: PREV200200041147  
 TITLE: Allo-dimeric class I MHC protein-induced tolerance by partial TCR engagement requires activation of an NKG2a-dependent inhibitory pathway of allo-reactive CD8+ T cells  
 AUTHOR: Wang, Hui, Chang, J. L.; Eiden, Robert A.; Trawick, Robert L.; Wang, J. L.; Li, J.; Wang, X. L.; Fan, J. H.; Wang, J. H.; Wang, Rong L.  
 CORPORATE OR IND: Department of Microbiology, University of Texas at Houston, Houston, TX, USA; e-mail: stephowski@uth.tmc.edu USA  
 SOURCE: Transplantation (Baltimore, April 27, 2002) Vol. 73, No. 7, pp. 1141-1148. http://www.transplantjournal.com/. print. ISSN: 0041-1136.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English

AB Background: The various toxicities associated with the general immune suppression resulting from current clinical immunosuppressive therapies continue to plague transplant recipients as well as jeopardize allograft survival. Methods: The present study utilized allochimeric class I MHC antigens (alphah u70-77-RT1.Aa) bearing only four donor RT1.Au polymorphic amino acids (a.a.; His70, Val73, Asn74, and Asn77) superimposed on the recipient RT1.Aa background to induce transplantation tolerance in the rat cardiac transplant model. Results: Oral delivery of alphah u70-77-RT1.Aa protein alone (days 0-4) induced tolerance, as evidenced by inhibition of both acute and chronic rejection processes. Delivery of alphah u70-77-RT1.Aa with therapeutic doses of cyclosporine (CsA) also prevented chronic rejection, otherwise readily developed after treatment with CsA alone. A polymerase chain reaction (PCR)-based analysis showed that tolerant recipients had a higher number of interleukin (IL)-10-producing CD4<sup>+</sup>CD25<sup>+</sup> splenic T helper (Th)1 cells and elevated numbers of IL-10<sup>+</sup>IL-12<sup>+</sup> splenic Th1 cells. Adoptive transfer experiments revealed that potent regulatory T cells mediated tolerance. The same T cells displayed diminished T cell receptor (TCR)-driven signaling via extracellular regulated kinase, AP-1, and NF-kappaB, as well as the common gamma-chain (gamma c) cytokine-receptor-induced signaling by Janus kinase 3 (Jak3)/stimulators and activators of transcription Stat/5 pathways. Tolerance induction was prevented in vivo by inhibition of signal 2 by CTLA4Ig or of signal 3 by either rapamycin, which disrupts the mammalian target of rapamycin, or AG490, which inhibits Jak3. Finally, partial or complete tyrosine phosphorylation of Jak3 was observed in alloantigen-specific T cell clones in response to tolerogenic versus immunogenic peptides, respectively. Conclusion: Tolerance induction by allochimeric proteins is achieved by partial TCR activation in the presence of signals 2 and 3, resulting in a skewed phenotype.

AB Dendritic cells (DC) constitute a complex system of multipotential, highly antigen-presenting cells that initiate and regulate adaptive immune responses.





DOCUMENT TYPE: Article  
LANGUAGE: English

A5 Bone marrow-derived dendritic cells (DCs) can be genetically engineered using adenoviral Ad vectors to express immunosuppressive molecules that promote T cell unresponsiveness. The success of these DCs for therapy of allograft rejection has been limited in part by the potential of the adenovirus to cause T cell activation and the inherent ability of the DCs to cross-present self and nonself antigens. An alternative to adenoviral delivery of immunosuppressive molecules is the use of adenoviral vectors that contain blocking agents for T cell activation, such as the combined use of NF-kappaB inhibitor, decoy receptor and CTLA4-Ig (Ad CTLA4-Ig) to generate stably immature myeloid DCs that secrete the potent costimulation blocking agent, Tumor Ad CTLA4-Ig-transduced ODN DCs exhibit markedly impaired allostimulatory ability and promote apoptosis of activated T cells. Furthermore, administration of Ad CTLA4-Ig ODN-treated donor DCs (C57BL/6; B10(H-2k)) before transplant significantly prolongs MHC-mismatched (C57BL/6; C57BL/6; C57BL/6; C57BL/6) vascularized heart allograft survival, with long-term (>100 days) donor-specific graft survival in 40% of recipients. The mechanism(s) responsible for DC tolerogenicity, which may involve activation-induced apoptosis of alloreactive T cells, do not lead to skewing of intragraft Th cytokine responses. Use of NF-kappaB antisense decoys in conjunction with Ad encoding a potent costimulation blocking agent offers promise for therapy of allograft rejection or autoimmune disease with minimization of systemic immunosuppression.

L6 ANSWER 5 OF 9 CELINE FARRINGTON 01/01/83

ACCESSION NUMBER: 100-2-20000

DOI: 10.1002/for

TITLE: The effect of tolerogenic dendritic cells for  
enhancing tolerogenicity in a CD4+ and  
CD8+ T cell mediated disease

INVENTOR(S): J. Johns, 1221 N. 1st Ave; Nino; Giannoukakis, Nick

PATENT ASSIGNMENT TO: University of Pittsburgh of the Commonwealth System of Higher Education, PA

SOURCE: FBI Int. April, 64 pp.

Table 1. *Continued*

DOCUMENT TYPE: Patent.

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICANT NAME	DATE
WO 2001093713	A1	20011114	W. A. 1-11-1991	1-1-1991
WO 2001093713	A1	20011114		

01	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY	AZ
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03	CA	CB	CC	CD	CE	CF	CG	CH	CI	CJ	CK	CL	CM	CN	CO	CP	CQ	CR	CS	CT	CV	CW	CX	CY	CZ	
04	DA	DB	DC	DD	DE	DF	DG	DH	DI	DJ	DK	DL	DM	DN	DO	DP	DQ	DR	DS	DT	DV	DW	DX	DY	DZ	
05	EA	EB	EC	ED	EE	EF	EG	EH	EI	EJ	EK	EL	EM	EN	EO	EP	EQ	ER	ES	ET	EV	EW	EX	EY	EZ	
06	FA	FB	FC	FD	FE	FF	FG	FH	FI	FJ	FK	FL	FM	FN	FO	FP	FQ	FR	FS	FT	FV	FW	FX	FY	FZ	
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08	HA	HB	HC	HD	HE	HF	HG	HH	HI	HJ	HK	HL	HM	HN	HO	HP	HQ	HR	HS	HT	HV	HW	HX	HY	HZ	
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12	LA	LB	LC	LD	LE	LF	LG	LH	LI	LJ	LK	LL	LM	LN	LO	LP	LQ	LR	LS	LT	LV	LW	LX	LY	LZ	
13	MA	MB	MC	MD	ME	MF	MG	MH	MI	MJ	MK	ML	MM	MN	MO	MP	MQ	MR	MS	MT	MV	MW	MX	MY	MZ	
14	NA	NB	NC	ND	NE	NF	NG	NH	NI	NJ	NK	NL	NM	NN	NO	NP	NQ	NR	NS	NT	NV	NW	NX	NY	NZ	
15	OA	OB	OC	OD	OE	OF	OG	OH	OI	OJ	OK	OL	OM	ON	OO	OP	OQ	OR	OS	OT	OV	OW	OX	OY	OZ	
16	PA	PB	PC	PD	PE	PF	PG	PH	PI	PJ	PK	PL	PM	PN	PO	PP	PQ	PR	PS	PT	PV	PW	PX	PY	PZ	
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21	UA	UB	UC	UD	UE	UF	UG	UH	UI	UJ	UK	UL	UM	UN	UO	UP	UQ	UR	US	UT	UV	UW	UX	UY	UZ	
22	VA	VB	VC	VD	VE	VF	VG	VH	VI	VJ	VK	VL	VM	VN	VO	VP	VQ	VR	VS	VT	VV	VW	VX	VY	VZ	
23	WA	WB	WC	WD	WE	WF	WG	WH	WI	WJ	WK	WL	WM	WN	WO	WP	WQ	WR	WS	WT	WV	WW	WX	WY	WZ	
24	XA	XB	XC	XD	XE	XF	XG	XH	XI	XJ	XK	XL	XM	XN	XO	XP	XQ	XR	XS	XT	XV	XW	XX	XY	XZ	
25	YA	YB	YC	YD	YE	YF	YG	YH	YI	YJ	YK	YL	YM	YN	YO</											

0001 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100  
 0002 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100  
 0003 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

$\frac{d}{dt} \left( \frac{1}{\rho} \right) = - \frac{1}{\rho^2} \frac{d\rho}{dt}$

A5 The present invention relates to a tolerogenic mammalian dendritic cell. The method for the production of the tolerogenic DCs. In addition, the present invention provides a method for enhancing tolerogenicity in a host comprising administering the tolerogenic mammalian cell to the present invention to the host. The tolerogenic DCs of the present invention surprise in that they are able to induce tolerance in a

NF- $\kappa$ B and p38 kinase sites. The **tolerogenic** role of the present invention may further comprise a viral vector, and preferably an adenoviral vector, which does not affect the **tolerogenicity** of the **tolerogenic** cells and present therein. Enhanced **tolerogenicity** of a host is useful for prolonging foreign graft survival and for treating inflammatory related diseases, such as autoimmune diseases.

16 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:922841 CAPLUS

DOCUMENT NUMBER: 137:45987

TITLE: The role of Stat5 in the induction of regulatory T cells in transplantation tolerance

AUTHOR(S): Stepkowski, S. M.; Kirgan, B. A.; Hany, A. A.; Trawick, R. W.; Wang, M.; Delgany, M.; Wang, M.-F.; Tian, L.; Clark, J.; Kiehl, K. L.

CORPORATE SOURCE: and Department of Infectious Biology, University of Texas, Houston, TX, USA

SOURCE: and transplantation tolerance of heart, 9-35-36; JHEP: 1998; 137: 45-46

PUBLISHER: and the Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The roles of extracellular-regulated kinase 2 (Erk2), NF- $\kappa$ B, AP-1, Janus tyrosine kinase (Jak3), and stimulators and activators of transcription 5 (Stat5) in mediating transplantation tolerance were studied. Tolerant recipients that had carried functional Wistar-Furth (WF) grafts for more than 100 days were rechallenged with a second WF heart. Purified T cells from spleens and lymph nodes of rejectors and tolerant T cells showed a significant increase in Jak3 expression. The presence of phosphorylated Erk2 and the expression of Jak3 indicated that the tolerant animals have actively reacting alloantigen-specific T cells, but that their response was distinct from that of nonactivated T cells of syngeneic grafts or fully activated T cells in rejectors. Tolerant T cells showed almost undetectable AP-1, NF- $\kappa$ B, and Stat5 DNA binding activities. The INF- $\gamma$  alone stimulated with immunogenic 9L- $\alpha$ - $\beta$  peptide showed potent Stat5 DNA binding activity (10<sup>4</sup> fold more by 10<sup>4</sup> fold). On the other hand, the INF- $\gamma$  alone stimulated with **tolerogenic** 9L- $\alpha$ - $\beta$  peptide showed almost undetectable DNA binding after 10<sup>4</sup> fold stimulation, and the Stat5 binding after 10<sup>4</sup> fold stimulation. These results indicated the existence of 10<sup>4</sup> fold more Stat5 binding activity in the tolerant TCR

REFERENCE COUNT: THERE ARE 1 CITE REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

16 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:922841 CAPLUS

DOCUMENT NUMBER: 137:45987

TITLE: Distinct mRNA and array profiles of **tolerogenic** dendritic cells

AUTHOR(S): Fusco-Poda Cortesini, N.; Giacca, F.; H, E.; Cibotario, R.; DeMasi, A.; Dalla-Favera, R.; Cortesini, R.

CORPORATE SOURCE: Department of Pathology, Columbia University, New York, NY, USA

SOURCE: and Immunology, 10-11, 12-13, 14-15

JHEP: 1998; 137: 45-46

PUBLISHER: and the Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Dendritic cells (DCs) are the most potent antigen-presenting cells (APCs) in the immune system. DCs are known to be involved in the induction of both **tolerogenic** and **immunogenic** responses. In this study, we have characterized the mRNA and array profiles of **tolerogenic** DCs. We found that **tolerogenic** DCs express a distinct set of genes, including **tolerogenic** markers such as **tolerogenic** markers.

changes occurring in **tolerogenic APC**, the mRNA profile of MD-1 dendritic cells exposed to allo-specific T helper and T suppressor cells were analyzed. This study now provides evidence that immature dendritic cells stimulated by T suppressor cells differentiate into mature dendritic cells with a distinct phenotype. The identification of the distinct pathways of dendritic cell differentiation is critical to the development of new therapeutic strategies.

REFERENCE COUNT: 11881 AND 11881 REFERENCES AVAILABLE FOR THIS REFERENCE. FULL-TEXT AVAILABLE IN THE REFERENCE

L6 ANSWER # 16 - 11881 AND 11881

ACCESSION NUMBER: 11881 AND 11881

DOCUMENT NUMBER: 11881 AND 11881

TITLE: Immunization of cardiac allograft survival using dendritic cells treated with NF- $\kappa$ B decoy oligodeoxynucleotides

AUTHOR: Hannekukh, Nick; Bonham, C. Andrew; Qian, Shiguang; Zhou, Zhongyou; Peng, Liansha; Harnaha, Jo; Li, Wei; Thomson, Angus W.; Fung, John J.; Robbins, Paul D.; Lu, Lina

CORPORATE SOURCE: Department of Molecular Genetics and Biochemistry, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: Molecular Therapy (2003), 16, Pt. 1, 44-48

CODEN: MTHCK; ISSN: 1525-0160

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

12 ANNOTATED BIBLIOGRAPHY BIOLOGICAL ABSTRACTS INC. UNPUBLISHED  
ACCESSION NUMBER: 1997-01-16-0000  
DOCUMENT NUMBER: 1997-01-16-0000  
TITLE: Manipulation of **dendritic cells** for tolerance induction in transplantation and autoimmune disease.

AUTHOR(S): Lu, Lina L.; Thomas, Anne M.  
CORPORATE SOURCE: 1) Thomas E. Starzl Transplantation Institute, University of Pittsburgh Medical Center, 355 Lothrop Street, E1554, Biomedical Science Tower, Pittsburgh, PA, 15261; LuL@msx.upmc.edu USA  
SOURCE: Transplantation (Baltimore), (January 15, 2002) Vol. 73, No. 1 Supplement, pp. S18-S22.  
<http://www.transplantationjournal.com/>, print.  
ISSN: 0041-1337.

DOCUMENT TYPE: General Review  
LANGUAGE: English

AB **Dendritic cells** (DC) are potent antigen-presenting cells that play a key role in the immune response. DCs have been shown to initiate and regulate immune responses. Recent studies have improved our understanding of DC development, differentiation, activation, and function. DC exist as distinct subsets that differ in their lineage affiliation, surface molecule expression, and biological function. These factors seem to determine the T-cell polarizing signals and type of T cell response-T helper 1, T helper 2, or T regulatory-induced by DC (1). Evidence has accumulated that DC play an important role in both central and peripheral tolerance via various mechanisms, including induction of T-cell anergy, immune deviation, T regulatory cell activity, and promotion of activated T-cell apoptosis. Although many of the details of the molecular basis of DC **tolerogenicity** have yet to be elucidated, emerging information suggests that costimulatory molecule deficiency, expression of death-inducing ligands (in particular Fas (CD95) ligand), microenvironmental factors (in particular anti-inflammatory/immunosuppressive cytokines), and inhibition of gene transcription regulatory proteins (e.g., nuclear factor-kappaB) can impact **tolerogenic** potential of DC (2). Manipulation of DC by control of their maturation and differentiation, or genetic engineering of these cells to express immunosuppressive molecules, offers potential for therapy of all graft rejection and autoimmune disease. In this review, we outline principles and techniques for generation of "tolerogenic" DC and summarize data that have been reported in experimental models. Space constraints limit discussion of clinical trials.

13 ANNOTATED BIBLIOGRAPHY BIOLOGICAL ABSTRACTS INC. UNPUBLISHED  
ACCESSION NUMBER: 1997-01-16-0000  
DOCUMENT NUMBER: 1997-01-16-0000  
TITLE: Marked proliferation of cardiac allograft survival by **dendritic cells** genetically engineered with NF-kappaB oligodeoxynucleotide decoys and adjuvant vaccines and IL-12/IL-18.

AUTHOR(S): Benhar, A.; Andrew, Lisa; Lian, Xinyan; Chen, Hongyan; Wang, Lian; Ma, Lili; Hackett, Hilary; Robbins, Paul D.; Thomas, Anne M.; Fung, John J.; Lu, Lina L.; Chikuma, Yu, Lina L.  
CORPORATE SOURCE: 1) Thomas E. Starzl Transplantation Institute, University of Pittsburgh Medical Center, 355 Lothrop Street, Biomedical Science Tower, E1554, Pittsburgh, PA, 15261; LuL@msx.upmc.edu USA  
SOURCE: Transplantation (Baltimore), (January 15, 2002) Vol. 73, No. 1 Supplement, pp. S23-S27.  
<http://www.transplantationjournal.com/>, print.  
ISSN: 0041-1337.

14 ANNOTATED BIBLIOGRAPHY BIOLOGICAL ABSTRACTS INC. UNPUBLISHED  
ACCESSION NUMBER: 1997-01-16-0000  
DOCUMENT NUMBER: 1997-01-16-0000  
TITLE: **Dendritic cells** (DC) are potent antigen-presenting cells that play a key role in the immune response. DCs have been shown to initiate and regulate immune responses. Recent studies have improved our understanding of DC development, differentiation, activation, and function. DC exist as distinct subsets that differ in their lineage affiliation, surface molecule expression, and biological function. These factors seem to determine the T-cell polarizing signals and type of T cell response-T helper 1, T helper 2, or T regulatory-induced by DC (1). Evidence has accumulated that DC play an important role in both central and peripheral tolerance via various mechanisms, including induction of T-cell anergy, immune deviation, T regulatory cell activity, and promotion of activated T-cell apoptosis. Although many of the details of the molecular basis of DC **tolerogenicity** have yet to be elucidated, emerging information suggests that costimulatory molecule deficiency, expression of death-inducing ligands (in particular Fas (CD95) ligand), microenvironmental factors (in particular anti-inflammatory/immunosuppressive cytokines), and inhibition of gene transcription regulatory proteins (e.g., nuclear factor-kappaB) can impact **tolerogenic** potential of DC (2). Manipulation of DC by control of their maturation and differentiation, or genetic engineering of these cells to express immunosuppressive molecules, offers potential for therapy of all graft rejection and autoimmune disease. In this review, we outline principles and techniques for generation of "tolerogenic" DC and summarize data that have been reported in experimental models. Space constraints limit discussion of clinical trials.

AB The present invention relates to a tolerogenic mammalian dendritic cells (DCs) and methods to use the same in the treatment of autoimmune diseases. In addition, the present invention provides a method for enhancing tolerogenicity in a host by administering the tolerogenic mammalian DCs of the present invention to the host. The tolerogenic DCs of the present invention comprise an anti- $\delta$  myelin basic protein (MBP) antibody, an anti-NP-398 antibody, or a combination thereof. The tolerogenic DCs of the present invention may further comprise a tolerogenic antigen, a tolerogenic adjuvant, or a combination thereof. The tolerogenic DCs of the present invention may be used to enhance tolerogenicity in a host.

the **tolerogenic** DCs when present therein. Enhanced **tolerogenicity** in a host is useful for prolonging tumor survival and for treating inflammatory-related diseases, such as autoimmune diseases.

LE ANSWER 4 OF 1 CAPLIN COPYRIGHT 2004 ACS  
ACCESSION NUMBER: 199194132  
DOCUMENT NUMBER: 19741410  
TITLE: **Tolerogenic dendritic cells**  
AUTHOR(S): **Chen, P. H.; Farsad, H.; Ilan, J.; Ho, E.; Chakrabarti, S.; Leshem, G.; Dalla-Favera, R.; Farsad, R.**  
CORPORATE SOURCE: Department of Pathology, Columbia University, New York, NY, USA  
SOURCE: **Humor. Immunology** 42(1), 62(10), 1065-1072  
CODEN: HUMIMY; ISSN: 0198-8959  
PUBLISHER: Elsevier Science Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB **Dendritic cells** are crucial to the activation as well as suppression of the immune response. Previous reports have illustrated that APC interacting with antigen-specific T suppressor cells become **tolerogenic**, inducing T helper anergy. To characterize the molecular changes occurring in **tolerogenic** APC, the mRNA profile of **MD-1 dendritic cells** exposed to allo-specific T helper and T suppressor cells was analyzed. This study now provides evidence that immature **dendritic cells** interacted by T suppressor cells with **MD-1 dendritic cells** with a distinct phenotype. The identification of the involved pathways of **dendritic cell** differentiation is critical to the development of new therapeutic strategies.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LE ANSWER 5 OF 1 CAPLIN COPYRIGHT 2004 ACS  
ACCESSION NUMBER: 199194132  
DOCUMENT NUMBER: 19741410  
TITLE: **Prolongation of cardiac allograft survival using dendritic cells treated with NF-kappa.B decoy oligodeoxynucleotides**  
AUTHOR(S): **Giannoukakis, Nick; Benham, C. Andrew; Han, Shihua; Zhou, Zhengyou; Peng, Lianshe; Harnaha, R.; Li, Wei; Thomson, Angus W.; Peng, Xian L.; Perkins, Paul L.; Li, Ling**  
CORPORATE SOURCE: Department of Molecular and Cellular Physiology, University of Pittsburgh, Pittsburgh, PA, USA  
SOURCE: **Journal of Heart and Lung Transplantation** 23(1), 41-47  
CODEN: JHLTDE; ISSN: 1047-1098  
PUBLISHER: Elsevier Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB **Dendritic cells** are highly potent APCs that help induce and regulate immune responses. Antigen-specific T cell responses are induced by stimulatory cells (CD40, CD80, CD86) and suppressed by inhibitory cells (B7-1, B7-2). Expression of these cells is associated with NF-kappa.B-dependent transcription of their genes. **Tolerogenicity** has been associated with impaired NF-kappa.B-dependent transcription of stimulatory genes as well as NF-kappa.B translocation to the nucleus. In this report, we demonstrate that double-stranded oligodeoxynucleotides (dsODNs) containing NF-kappa.B (NF-kappa.B-DNA) are critically important for marrow-derived T cell-specifically induced NF-kappa.B-dependent

transcription of a reported gene. Moreover, exposure of DC to the oxygenation of bone marrow conditioned by lipopolysaccharide (LPS)-induced nitric oxide primarily, a major inhibitor of Th1 differentiation. Treatment of bone marrow-derived DC produced with NF-kappa.B DNA covalently suppressed the cell-surface expression of costimulatory molecules without interfering with MHC class II or class II expression. Furthermore, NF-kappa.B ODN DC induced allogeneic donor-specific hyporesponsiveness in mixed leukocyte cultures, and this was associated with inhibition of Th1-type cytokine production. Finally, infusion of NF-kappa.B ODN-modified bone marrow-derived DC into allogeneic recipients prior to heart transplantation resulted in significant prolongation of allograft survival in the absence of immunosuppression. Specific interference with NF-kappa.B and other transcriptional pathways involved in immune stimulation in DC using all decoy approaches could be the means to promote tolerance induction in organ transplantation. (S. J. Freeman) (1)

REFERENCE COUNT: 11 THREE ARE CITED REFERENCES AVAILABLE FOR THIS REFERENCE AND REMAINING AVAILABLE IN THE CD FORMAT